ANTISENSE MODULATION OF MICROSOMAL PROSTAGLANDIN E2 SYNTHASE EXPRESSION

The present application claims priority under Title 35, United States Code, §119 to United States Provisional application Serial No. 60/413,549, filed September 25, 2002, which is incorporated by reference in its entirety as if written herein.

FIELD OF THE INVENTION

[001] The present invention provides compositions and methods for modulating the expression of Microsomal Prostaglandin E2 Synthase (mPGES-1). In particular, this invention relates to antisense compounds, particularly oligonucleotides, specifically hybridizable with nucleic acids encoding mPGES-1. Such oligonucleotides have been shown to modulate the expression of mPGES-1.

BACKGROUND OF THE INVENTION

[002] Prostaglandin H_2 (PGH_2) produced by COX-2 is ultimately converted to a variety of products, some of which are PGE_2, PGD_2, and PGI2 (prostacyclin). All of these compounds are made by downstream syntheses, which have been identified (Urade et al, *J Lipid Mediat Cell Signal.* 1995 Oct;12(2-3):257-73. et al, 1995). However, *in vitro* PGH_2 will also spontaneously convert to a mixture of predominantly PGE_2 and a small amount of PGD_2, although the rate of this reaction is several orders of magnitude slower than the enzymatic conversion.

[003] It has recently been shown that there are two forms of PGE_2 synthase, microsomal (mPGES-1) (also referred to as Pig-12 and PTGES) and cytosolic (cPGE2S). It has been shown that there is a form of the PGE_2S enzyme in macrophages inducible by LPS (Matsumoto et al, *Biochem Biophys Res Commun.* 1997 Jan 3;230(1):110-4). Resting macrophages form a wide variety of products (TXB_2, PGD_2 and PGE_2) that are primarily produced from

the PGH_2 formed by COX-1. Upon induction of COX-2 and mPGES-1 by LPS, the primary product is PGE_2.

[004] Recently it has also been found that the inducible PGES is a microsomal, glutathione-dependent enzyme whose induction is down regulated by dexamethasone (Jakobsson et al, *Proc Natl Acad Sci U S A.* 1999 Jun 22;96(13):7220-5).

[005] A549 cells, a human lung adenocarcinoma-derived cell line, contain a PGE_2S that is inducible by IL-1b and TNFa. This expression is concurrent with COX-2 expression and PGE_2 production. This expression was also down regulated by dexamethasone. These cells were used in an enzyme assay that was developed to specifically look at the conversion of PGH_2 to PGE_2. NS-398 was found to inhibit PGE_2S at 20 uM, sulindac sulfide at 80 uM and LTC4 at 5 uM (Jakobsson et al, *Proc Natl Acad Sci U S A.* 1999 Jun 22;96(13):7220-5; Thoren et al, *Eur J Biochem.* 2000 Nov;267(21):6428-34).

[006] Rat mPGES-1-1 synthase has recently been cloned from peritoneal macrophages incubated with LPS (Murakami et al, *J Biol Chem.* 2000 Oct 20;275(42):32783-92). The gene encoding the found to have high homology to the previously described protein MAPEG-L1 (Membrane Associated Proteins in Eicosanoid and Glutathione metabolism- Like 1) (Jakobsson et al, *Protein Sci.* 1999 Mar;8(3):689-92) and that it is a member of the MAPEG-1 superfamily of proteins that include microsomal GST's, LTC_4 synthase and 5-lipoxygenase activating protein or FLAP (Jakobsson et al, *Am J Respir Crit Care Med.* 2000 Feb;161(2 Pt 2):S20-4).

[007] The protein encoded by the cDNA is a 153 AA protein. The rat form was found to have 80% sequence identity to the human form. Confocal microscopy experiments showed co-localization of PGE2S and COX-2. Rat inducible PGE_2S has been cloned and expressed in CHO cells and used in an enzyme assay (Mancini, et al, *J Biol Chem* 2001 Feb 9;276(6):4469-75). The LTC4 synthase inhibitor MK-886 inhibited PGE_2S with an IC_{50} of 3.4 uM.

[008] mPGES-1 expression has been established in human colon cancer tumors (Yoshimatsu et al, *Clinical Cancer Research* (7) 3971-3976, 2001) and small cell lung cancer cells (Yoshimatsu et al, *Clin Cancer Res* 2001 Sep.

7(9):2669-74). >80% of all tumors tested positive for both COX-2 and mPGES-1, suggesting a requirement of overexpressed mPGES-1 for production of PGE_2.

[009] A cytosolic form of PGE_2S that is functionally coupled with COX-1 has recently been identified (Tanioka et al, *J Biol Chem.* 2000 Oct 20;275(42):32775-82). The protein identified (cPGES) is a glutathione-dependent cytosolic enzyme found in rat brains. Peptide sequencing revealed that it was identical to the previously described p23, a component of the steroid hormone/HSP-90 complex. Recombinant expression of p23 in E. coli and 293 cells produced a functional PGE_2 synthase. This protein is constitutively expressed and evidence suggests that it is coupled to COX-1. Hence it appears that there are both constitutive and inducible forms of PGE_2S encoded by distinctly different genes and are linked respectively to the constitutive and inducible forms of cyclooxygenase.

[0010] The role of PGE_2 in inflammation has been well established. Monoclonal anti-bodies to PGE_2 have been shown to be as efficacious in an animal model of hyperalgesia and pain as COX-2 inhibition alone (Zhang et al, *J Pharmacol Exp Ther* 1997 Dec;283(3):1069-75) suggesting that PGE_2 is the major pro-inflammatory cytokine and inhibition of PGE_2 alone is sufficient for an anti-inflammatory therapy.

[0011] Antisense technology is emerging as an effective means for reducing the expression of specific gene products and may therefore prove to be uniquely useful in a number of therapeutic, diagnostic, and research applications for the modulation of mPGES-1 expression.

SUMMARY OF THE INVENTION

[0012] The present invention is directed to antisense compounds, particularly oligonucleotides, which are targeted to a nucleic acid encoding mPGES-1, and which modulate the expression of mPGES-1. Pharmaceutical and other compositions comprising the antisense compounds of the invention are also provided. Further provided are methods of modulating the expression of mPGES-1 in cells or tissues comprising contacting said cells or tissues with one or more of the antisense compounds or compositions of the invention. Further

provided are methods of treating an animal, particularly a human, suspected of having or being prone to a disease or condition associated with expression of mPGES-1 by administering a therapeutically or prophylactically effective amount of one or more of the antisense compounds or compositions of the invention.

DETAILED DESCRIPTION OF THE INVENTION

[0013] The present invention employs oligomeric antisense compounds, particularly oligonucleotides, for use in modulating the function of nucleic acid molecules encoding mPGES-1, ultimately modulating the amount of mPGES-1 produced. This is accomplished by providing antisense compounds, which specifically hybridize with one or more nucleic acids encoding mPGES-1. As used herein, the terms "target nucleic acid" and "nucleic acid encoding mPGES-1" encompass DNA encoding mPGES-1, RNA (including pre-mRNA and mRNA) transcribed from such DNA, and also cDNA derived from such RNA. The specific hybridization of an oligomeric compound with its target nucleic acid interferes with the normal function of the nucleic acid. This modulation of function of a target nucleic acid by compounds, which specifically hybridize to it, is generally referred to as "antisense". The functions of DNA to be interfered with include replication and transcription. The functions of RNA to be interfered with include all vital functions such as, for example, translocation of the RNA to the site of protein translation, translation of protein from the RNA, splicing of the RNA to yield one or more mRNA species, and catalytic activity which may be engaged in or facilitated by the RNA. The overall effect of such interference with target nucleic acid function is modulation of the expression of mPGES-1. In the context of the present invention, "modulation" means either an increase (stimulation) or a decrease (inhibition) in the expression of a gene. In the context of the present invention, inhibition is the preferred form of modulation, of gene expression and mRNA is a preferred target.

[0014] It is preferred to target specific nucleic acids for antisense. "Targeting" an antisense compound to a particular nucleic acid, in the context of this invention, is a multistep process. The process usually begins with the

identification of a nucleic acid sequence whose function is to be modulated. This may be, for example, a cellular gene (or mRNA transcribed from the gene) whose expression is associated with a particular disorder or disease state, or a nucleic acid molecule from an infectious agent. In the present invention, the target is a nucleic acid molecule encoding mPGES-1. The targeting process also includes determination of a site or sites within this gene for the antisense interaction to occur such that the desired effect, e.g., detection or modulation of expression of the protein, will result. Within the context of the present invention, a preferred intragenic site is the region encompassing the translation initiation or termination codon of the open reading frame (ORF) of the gene. Since, as is known in the art, the translation initiation codon is typically 5'-AUG (in transcribed mRNA molecules; 5'-ATG in the corresponding DNA molecule), the translation initiation codon is also referred to as the "AUG codon," the "start codon" or the "AUG start codon". A minority of genes have a translation initiation codon having the RNA sequence 5'-GUG, 5'-UUG or 5'-CUG, and 5'-AUA, 5'-ACG and 5'-CUG have been shown to function in vivo. Thus, the terms "translation initiation codon" and "start codon" can encompass many codon sequences, even though the initiator amino acid in each instance is typically methionine (in eukaryotes) or formylmethionine (in prokaryotes). It is also known in the art that eukaryotic and prokaryotic genes may have two or more alternative start codons, any one of which may be preferentially utilized for translation initiation in a particular cell type or tissue, or under a particular set of conditions. In the context of the invention, "start codon" and "translation initiation codon" refer to the codon or codons that are used in vivo to initiate translation of an mRNA molecule transcribed from a gene encoding mPGES, regardless of the sequence(s) of such codons.

[0015] It is also known in the art that a translation termination codon (or "stop codon") of a gene may have one of three sequences, i.e. 5'-UAA, 5'-UAG and 5'-UGA (the corresponding DNA sequences are 5'-TAA, 5'-TAG and 5'-TGA, respectively). The terms "start codon region" and "translation initiation codon region "refer to a portion of such an mRNA or gene that encompasses from about 25 to about 50 contiguous nucleotides in either direction (i.e., 5' or 3') from a translation initiation codon. Similarly, the terms "stop codon region"

and "translation termination codon region "refer to a portion of such an mRNA or gene that encompasses from about 25 to about 50 contiguous nucleotides in either direction (i.e., 5' or 3') from a translation termination codon.

[0016] The open reading frame (ORF) or "coding region," which is known in the art to refer to the region between the translation initiation codon and the translation termination codon, is also a region which may be targeted effectively. Other target regions include the 5' untranslated region (5'UTR), known in the art to refer to the portion of an mRNA in the 5' direction from the translation initiation codon, and thus including nucleotides between the 5' cap site and the translation initiation codon of an mRNA or corresponding nucleotides on the gene, and the 3' untranslated region (3'UTR), known in the art to refer to the portion of an mRNA in the 3' direction from the translation termination codon, and thus including nucleotides between the translation termination codon and 3' end of an mRNA or corresponding nucleotides on the gene. The 5' cap of an mRNA comprises an N7-methylated guanosine residue joined to the 5'-most residue of the mRNA via a 5'-5' triphosphate linkage. The 5' cap region of an mRNA is considered to include the 5' cap structure itself as well as the first 50 nucleotides adjacent to the cap. The 5' cap region may also be a preferred target region.

[0017] Although some eukaryotic mRNA transcripts are directly translated, many contain one or more regions, known as "introns," which are excised from a transcript before it is translated. The remaining (and therefore translated) regions are known as "exons" and are spliced together to form a continuous mRNA sequence. mRNA splice sites, i.e., intron-exon junctions, may also be preferred target regions, and are particularly useful in situations where aberrant splicing is implicated in disease, or where an overproduction of a particular mRNA splice product is implicated in disease. Aberrant fusion junctions due to rearrangements or deletions are also preferred targets. It has also been found that introns can also be effective, and therefore preferred, target regions for antisense compounds targeted, for example, to DNA or pre-mRNA.

[0018] Once one or more target sites have been identified, oligonucleotides are chosen which are sufficiently complementary to the target, i.e., hybridize sufficiently well and with sufficient specificity, to give the desired effect.

[0019] In the context of this invention, "hybridization" means hydrogen bonding, which may be Watson-Crick, Hoogsteen, or reversed Hoogsteen hydrogen bonding, between complementary nucleoside or nucleotide bases. For example, adenine and thymine are complementary nucleobases, which pair through the formation of hydrogen bonds. "Complementary," as used herein, refers to the capacity for precise pairing between two nucleotides. For example, if a nucleotide at a certain position of an oligonucleotide is capable of hydrogen bonding with a nucleotide at the same position of a DNA or RNA molecule, then the oligonucleotide and the DNA or RNA are considered to be complementary to each other at that position. The oligonucleotide and the DNA or RNA are complementary to each other when a sufficient number of corresponding positions in each molecule are occupied by nucleotides which can hydrogen bond with each other. Thus, "specifically hybridizable" and "complementary" are terms which are used to indicate a sufficient degree of complementarity or precise pairing such that stable and specific binding occurs between the oligonucleotide and the DNA or RNA target. It is understood in the art that the sequence of an antisense compound need not be 100% complementary to that of its target nucleic acid to be specifically hybridizable. An antisense compound is specifically hybridizable when binding of the compound to the target DNA or RNA molecule interferes with the normal function of the target DNA or RNA to cause a loss of utility, and there is a sufficient degree of complementarity to avoid non-specific binding of the antisense compound to non-target sequences under conditions in which specific binding is desired, i.e., under physiological conditions in the case of in vivo assays or therapeutic treatment, and in the case of in vitro assays, under conditions in which the assays are performed.

[0020] Antisense compounds are commonly used as research reagents and diagnostics. For example, antisense oligonucleotides, which are able to inhibit gene expression with exquisite specificity, are often used by those of ordinary skill to elucidate the function of particular genes. Antisense compounds are also used, for example, to distinguish between functions of various members of a biological pathway. Antisense modulation has, therefore, been harnessed for research use.

[0021] The specificity and sensitivity of antisense is also harnessed by those of skill in the art for therapeutic uses. Antisense oligonucleotides have been employed as therapeutic moieties in the treatment of disease states in animals and man. Antisense oligonucleotides have been safely and effectively administered to humans and numerous clinical trials are presently underway. It is thus established that oligonucleotides can be useful therapeutic modalities that can be configured to be useful in treatment regimes for treatment of cells, tissues and animals, especially humans. In the context of this invention, the term "oligonucleotide" refers to an oligomer or polymer of ribonucleic acid (RNA) or deoxyribonucleic acid (DNA) or mimetics thereof. This term includes oligonucleotides composed of naturally occurring nucleobases, sugars and covalent internucleoside (backbone) linkages as well as oligonucleotides having non-naturally occurring portions which function similarly. Such modified or substituted oligonucleotides are often preferred over native forms because of desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for nucleic acid target and increased stability in the presence of nucleases.

[0022] While antisense oligonucleotides are a preferred form of antisense compound, the present invention comprehends other oligomeric antisense compounds, including but not limited to oligonucleotide mimetics such as are described below. The antisense compounds in accordance with this invention preferably comprise from about 8 to about 30 nucleobases (i.e. from about 8 to about 30 linked nucleo sides). Particularly preferred antisense compounds are antisense oligonucleotides, even more preferably those comprising from about 12 to about 25 nucleobases. As is known in the art, a nucleoside is a base-sugar combination. The base portion of the nucleoside is normally a heterocyclic base. The two most common classes of such heterocyclic bases are the purines and the pyrimidines. Nucleotides are nucleosides that further include a phosphate group covalently linked to the sugar portion of the nucleoside. For those nucleosides that include a pentofuranosyl sugar, the phosphate group can be linked to either the 2', 3' or 5' hydroxyl moiety of the sugar. In forming oligonucleotides, the phosphate groups covalently link adjacent nucleosides to one another to form a linear polymeric compound. In turn the respective ends of

this linear polymeric structure can be further joined to form a circular structure, however, open linear structures are generally preferred. Within the oligonucleotide structure, the phosphate groups are commonly referred to as forming the internucleoside backbone of the oligonucleotide. The normal I linkage or backbone of RNA and DNA is a 3' to 5' phosphodiester linkage.

[0023] Specific examples of preferred antisense compounds useful in this invention include oligonucleotides containing modified backbones or non-natural internucleoside linkages. As defined in this specification, oligonucleotides having modified backbones include those that retain a phosphorus atom in the backbone and those that do not have a phosphorus atom in the backbone. For the purposes of this specification, and as sometimes referenced in the art, modified oligonucleotides that do not have a phosphorus atom in their internucleoside backbone can also be considered to be oligonucleosides.

[0024] Preferred modified oligonucleotide backbones include, for example, phosphorothioates, chiral phosphorothioates, phosphorodithioates, phosphotriesters, aminoalkylphosphotriesters, methyl and other alkyl phosphonates including 3'alkylene phosphonates and chiral phosphonates, phosphinates, phosphoramidates including 3'-amino phosphoramidate and aminoalkylphosphoramidates, thionophosphoramidates, thionoalkylphosphonates, thionoalkylphosphotriesters, and boranophosphates having normal 3'-5' linkages, 2'-5' linked analogs of these, and those having inverted polarity wherein the adjacent pairs of nucleoside units are linked 3'-5' to 5'-3' or 2'-5' to 5'-2'. Various salts, mixed salts and free acid forms are also included.

[0025] Representative United States patents that teach the preparation of the above phosphorus-containing linkages include, but are not limited to, U.S. 3,687,808; 4,469,863; 4,476,301; 5,023,243; 5,177,196; 5,188,897; 5,264,423; 5,276,019; 5,278,302; 5,286,717; 5,321,131; 5,399,676; 5,405,939; 5,453,496; 5,455,233; 5,466,677; 5,476,925; 5,519,126; 5,536,821; 5,541,306; 5,550,111; 5,563,253; 5,571,799; 5,587,361; and 5,625,050, each of which is herein incorporated by reference.

[0026] Preferred modified oligonucleotide backbones that do not include a phosphorus atom therein have backbones that are formed by short chain alkyl or cycloalkyl internucleoside linkages, mixed heteroatom and alkyl or cycloalkyl internucleoside linkages, or one or more short chain heteroatomic or heterocyclic internucleoside linkages. These include those having morpholino linkages (formed in part from the sugar portion of a nucleoside); siloxane backbones; sulfide, sulfoxide and sulfone backbones; formacetyl and thioformacetyl backbones; methylene formacetyl and thioformacetyl backbones; alkene containing backbones; sulfamate backbones; methyleneimino and methylenehydrazino backbones; sulfonate and sulfonamide backbones; amide backbones; and others having mixed N, O, S and CH_2 component parts.

[0027] Representative United States patents that teach the preparation of the above oligonucleosides include, but are not limited to, U.S. 5,034,506; 5,166,315; 5,185,444; 5,214,134; 5,216,141; 5,235,033; 5,264,562; 5,264,564; 5,405,938; 5,434,257; 5,466,677; 5,470,967; 5,489,677; 5,541,307; 5,561,225; 5,596,086; 5,602,240; 5,610,289; 5,602,240; 5,608,046; 5,610,289; 5,618,704; 5,623,070; 5,663,312; 5,633,360; 5,677,437; and 5,677,439, each of which is herein incorporated by reference.

[0028] In other preferred oligonucleotide mimetics, both the sugar and the internucleoside linkage, i.e., the backbone, of the nucleotide units are replaced with novel groups. The base units are maintained for hybridization with an appropriate nucleic acid target compound. One such oligomeric compound, an oligonucleotide mimetic that has been shown to have excellent hybridization properties, is referred to as a peptide nucleic acid (PNA). In PNA compounds, the sugar-backbone of an oligonucleotide is replaced with an amide containing backbone, in particular an aminoethylglycine backbone. The nucleobases are retained and are bound directly or indirectly to aza nitrogen atoms of the amide portion of the backbone. Representative United States patents that teach the preparation of PNA compounds include, but are not limited to, U.S. 5,539,082; 5,714,331; and 5,719,262, each of which is herein incorporated by reference. Further teaching of PNA compounds can be found in Nielsen et al., *Science*, 1991, 254, 1497-1500.

[0029] Most preferred embodiments of the invention are oligonucleotides with phosphorothioate backbones and oligonucleosides with heteroatom backbones, and in particular -CH_2-NH-O-CH_2-, -CH_2-N (CH_3) -O-CH_2- [known as a methylene (methylimino) or MMI backbone], - CH_2-O-N (CH_3) -CH_2-, - $CH_2N(CH_3)$-$N(CH_3)$-CH_2- and -O-$N(CH_3)$-CH_2-CH_2- [wherein the native phosphodiester backbone is represented as -O-P-O-CH_2-] of the above referenced U.S. patent 5,489,677, and the amide backbones of the above referenced U.S. patent 5,602,240. Also preferred are oligonucleotides having morpholino backbone structures of the above-referenced U.S. patent 5,034,506.

[0030] Modified oligonucleotides may also contain one or more substituted sugar moieties. Preferred oligonucleotides comprise one of the following at the 2' position: OH; F; O-, S-, or N-alkyl; O-, S-, or N-alkenyl; O-, S- or N-alkynyl; or O-alkyl-O-alkyl, wherein the alkyl, alkenyl and alkynyl may be substituted or unsubstituted C_1 to C_{10} alkyl or C_2 to C_{10} alkenyl and alkynyl. Particularly preferred are $O[(CH_2)_nO]_mCH_3$, $O(CH_2)_n,OCH_3$, $O(CH_2)_nNH_2$, $O(CH_2)_nCH_3$, $O(CH_2)_nONH_2$, and $O(CH_{2n}ON[(CH_2)_nCH_3)]_2$ where n and m are from 1 to about 10. Other preferred oligonucleotides comprise one of the following at the 2' position: C_1 to C_{10}, (lower alkyl, substituted lower alkyl, alkaryl, aralkyl, O-alkaryl or O-aralkyl, SH, SCH_3, OCN, Cl, Br, CN, CF_3, OCF_3, $SOCH_3$, SO_2CH_3, ONO_2, NO_2, N_3, NH_2, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino, substituted silyl, an RNA cleaving group, a reporter group, an intercalator, a group for improving the pharmacokinetic properties of an oligonucleotide, or a group for improving the pharmacodynamic properties of an oligonucleotide, and other substituents having similar properties. A preferred modification includes 2' -methoxyethoxy (2' -O-$CH_2CH_2OCH_3$, also known as 2'-O- (2-methoxyethyl) or 2'-MOE) (Martin et al., *Helv. Chim. Acta*, 1995, 78, 486-504) i.e., an alkoxyalkoxy group. A further preferred modification includes 2'-dimethylaminooxyethoxy, i.e., an $O(CH_2)_2ON(CH_3)_2$ group, also known as 2'-DMAOE, as described in examples herein below, and 2'-dimethylaminoethoxyethoxy (also known in the art as 2'-O-dimethylaminoethoxyethyl or 2'-DMAEOE), i.e., 2'-O-CH_2-O-CH_2-N $(CH_2)_2$, also described in examples herein below.

[0031] Other preferred modifications include 2'-methoxy (2'-O CH_3), 2'-aminopropoxy (2'-O CH_2 CH_2 CH_2NH_2) and 2'-fluoro (2'-F). Similar modifications may also be made at other positions on the oligonucleotide, particularly the 3' position of the sugar on the 3' terminal nucleotide or in 2'-5' linked oligonucleotides and the 5' position of 5' terminal nucleotide. Oligonucleotides may also have sugar mimetics such as cyclobutyl moieties in place of the pentofuranosyl sugar. Representative United States patents that teach the preparation of such modified sugar structures include, but are not limited to, U.S.: 4,981,957; 5,118,800; 5,319,080; 5,359,044; 5,393,878; 5,446,137; 5,466,786; 5,514,785; 5,519,134; 5,567,811; 5,576,427; 5,591,722; 5,597,909; 5,610,300; 5,627,053; 5,639,873; 5,646,265; 5,658,873; 5,670,633; and 5,700,920, each of which is herein incorporated by reference in its entirety.

[0032] Oligonucleotides may also include nucleobase (often referred to in the art simply as "base") modifications or substitutions. As used herein, "unmodified" or "natural" nucleobases include the purine bases adenine (A) and guanine (G), and the pyrimidine bases thymine (T), cytosine (C) and uracil (U). Modified nucleobases include other synthetic and natural nucleobases such as 5-methylcytosine (5-me-C), 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl and other alkyl derivatives of adenine and guanine, 2-propyl and other alkyl derivatives of adenine and guanine, 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-halouracil and cytosine, 5-propynyl uracil and cytosine, 6-azo uracil, cytosine and thymine, 5-uracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl and other 8-substituted adenines and guanines, 5-halo particularly 5-bromo, 5-trifluoromethyl and other 5-substituted uracils and cytosines, 7-methylquanine and 7-methyladenine, 8-azaguanine and 8-azaadenine, 7-deazaguanine and 7-deazaadenine and 3-deazaguanine and 3-deazaadenine. Further nucleobases include those disclosed in United States Patent No. 3,687,808, those disclosed in *The Concise Encyclopedia Of Polymer Science And Engineering*, pages 858-859, Kroschwitz, J.I., ed. John Wiley & Sons, 1990, those disclosed by Englisch et al., *Angewandte Chemie*, International Edition, 1991, 30, 613, and those disclosed by Sanghvi, Y.S., Chapter 15, *Antisense Research and Applications*, pages 289-302, Crooke, S.T. and Lebleu, B. ed., CRC Press, 1993. Certain of

these nucleobases are particularly useful for increasing the binding affinity of the oligomeric compounds of the invention. These include 5-substituted pyrimidines, 6-azapyrimidines and N-2, N-6 and O-6 substituted purines, including 2-aminopropyladenine, 5-propynyluracil and 5-propynylcytosine. 5-methylcytosine substitutions have been shown to increase nucleic acid duplex stability by 0.6-1.2°C (Sanghvi, Y.S., Crooke, S.T. and Lebleu, B., eds, *Antisense Research and Applications*, CRC Press, Boca Raton, 1993, pp. 276-278) and are presently preferred base substitutions, even more particularly when combined with 2'-O-methoxyethyl sugar modifications.

[0033] Representative United States patents that teach the preparation of certain of the above noted modified nucleobases as well as other modified nucleobases include, but are not limited to, the above noted U.S. 3,687,808, as well as U.S. 4,845,205; 5,130,302; 5,134,066; 5,175,273; 5,367,066; 5,432,272; 5,457,187; 5,459,255; 5,484,908; 5,502,177; 5,525,711; 5,552,540; 5,587,469; 5,594,12', 5,596,091; 5,614,617; 5,750,629; and 5,681,941, each of which is herein incorporated by reference.

[0034] Another modification of the oligonucleotides of the invention involves chemically linking to the oligonucleotide one or more moieties or conjugates, which enhance the activity, cellular distribution, or cellular uptake of the oligonucleotide. Such moieties include but are not limited to lipid moieties such as a cholesterol moiety (Letsinger et al., *Proc. Natl. Acad. Sci. USA*, 1989, 86, 6553-6556), cholic acid (Manoharan et al., *Bioorg. Med. Chem. Let.*, 1994, 4, 1053-1060), a thioether, e.g., hexyl-S-tritylthiol (Manoharan et al., *Ann. N.Y. Acad. Sci.*, 1992, 660, 306-309; Manoharan et al., *Bioorg. Med. Chem. Let.*, 1993, 3, 2765-2770), a thiocholesterol (Oberhauser et al., *Nucl. Acids Res.*, 1992, 20, 533-538), an aliphatic chain, e.g., dodecandiol or undecyl residues (Saison-Behmoaras et al., *EMBO J.*, 1991, 10, 1111-1118; Kabanov et al., *FEBS Lett.*, 1990, 259, 327-330; Svinarchuk et al., *Biochimie*, 1993, 75, 49-54), a phospholipid, e.g., di-hexadecyl-rac-glycerol or triethylammonium 1,2-di-O-hexadecyl-rac-glycero-3-H-phosphonate (Manoharan et al., *Tetrahedron Lett.*, 1995, 36, 3651-3654; Shea et al., *Nucl. Acids Res.*, 1990, 18, 3777-3783), a polyamine or a polyethylene glycol chain (Mancharan et al., *Nucleosides & Nucleotides*, 1995, 14, 969-973), or adamantane acetic acid (Manoharan et al.,

Tetrahedron Lett., 1995, 36, 365'-3654), a palmityl moiety (Mishra et al., *Biochim. Biophys. Acta*, 1995, 1264, 229-237), or an octadecylamine or hexylamino-carbonyl-oxycholesterol moiety (Crooke et al., *J. Pharmacol. Exp. Ther.*, 1996, 277, 923-937).

[0035] Representative United States patents that teach the preparation of such oligonucleotide conjugates include, but are not limited to, U.S. 4,828,979; 4,948,882; 5,218,105; 5,525,465; 5,541,313; 5,545,730; 5,552,538; 5,578,717, 5,580,731; 5,580,731; 5,591,584; 5,109,124; 5,118,802; 5,138,045; 5,414,077; 5,486,603; 5,512,439; 5,578,718; 5,608,046; 4,587,044; 4,605,735; 4,667,025; 4,762,779; 4,789,737; 4,824,941; 4,835,263; 4,876,335; 4,904,582; 4,958,013; 5,082,830; 5,112,963; 5,214,136; 5,082,830; 5,112,963; 5,214,136; 5,245,022; 5,254,469; 5,258,506; 5,262,536; 5,272,250; 5,292,873; 5,317,098; 5,371,241, 5,391,723; 5,416,203, 5,451,463; 5,510,475; 5,512,667; 5,514,785; 5,565,552; 5,567,810; 5,574,142; 5,585,481; 5,587,371; 5,595,726; 5,597,696; 5,599,923; 5,599,928 and 5,688,941, each of which is herein incorporated by reference.

[0036] It is not necessary for all positions in a given compound to be uniformly modified, and in fact more than one of the aforementioned modifications may be incorporated in a single compound or even at a single nucleoside within an oligonucleotide. The present invention also includes antisense compounds, which are chimeric compounds. "Chimeric" antisense compounds or "chimeras," in the context of this invention, are antisense compounds, particularly oligonucleotides, which contain two or more chemically distinct regions, each made up of at least one monomer unit, i.e., a nucleotide in the case of an oligonucleotide compound. These oligonucleotides typically contain at least one region wherein the oligonucleotide is modified so as to confer upon the oligonucleotide increased resistance to nuclease degradation, increased cellular uptake, and/or increased binding affinity for the target nucleic acid. An additional region of the oligonucleotide may serve as a substrate for enzymes capable of cleaving RNA:DNA or RNA:RNA hybrids. By way of example, RNase H is a cellular endonuclease, which cleaves the RNA strand of RNA:DNA duplex. Activation of RNase H, therefore, results in cleavage of the RNA target, thereby greatly enhancing the efficiency of oligonucleotide inhibition of gene expression. Consequently, comparable results

can often be obtained with shorter oligonucleotides when chimeric oligonucleotides are used, compared to phosphorothioate deoxyoligonucleotides hybridizing to the same target region. Cleavage of the RNA target can be routinely detected by gel electrophoresis and, if necessary, associated nucleic acid hybridization techniques known in the art.

[0037] Chimeric antisense compounds of the invention may be formed as composite structures of two or more oligonucleotides, modified oligonucleotides, oligonucleosides and/or oligonucleotide mimetics as described above. Such compounds have also been referred to in the art as hybrids or gapmers. Representative United States patents that teach the preparation of such hybrid structures include, but are not limited to, U.S. 5,013,830; 5,149,797; 5,220,007; 5,256,775; 5,366,878; 5,403,711; 5,491,133; 5,565,350; 5,623,065; 5,652,355; 5,652,356; and 5,700,922, certain of which are commonly owned with the instant application, and each of which is herein incorporated by reference in its entirety.

[0038] The antisense compounds used in accordance with this invention may be conveniently, and routinely made through the well-known technique of solid phase synthesis. Equipment for such synthesis is sold by several vendors including, for example, Applied Biosystems (Foster City, CA). Any other means for such synthesis known in the art may additionally or alternatively be employed. It is well known to use similar techniques to prepare oligonucleotides such as the phosphorothioates and alkylated derivatives.

[0039] The antisense compounds of the invention are synthesized in vitro and do not include antisense compositions of biological origin, or genetic vector constructs designed to direct the in vivo synthesis of antisense molecules. The compounds of the invention may also be admixed, encapsulated, conjugated or otherwise associated with other molecules, molecule structures or mixtures of compounds, as for example, liposomes, receptor targeted molecules, oral, rectal, topical or other formulations, for assisting in uptake, distribution and/or absorption. Representative United States patents that teach the preparation of such uptake, distribution and/or absorption assisting formulations include, but are not limited to, U.S. 5,108,921; 5,354,844; 5,416,016; 5,459,127; 5,521,291; 5,543,158; 5,547,932; 5,583,020; 5,591,721; 4,426,330; 4,534,899; 5,013,556;

5,108,921; 5,213,804; 5,227,170; 5,264,221; 5,356,633; 5,395,619; 5,416,016; 5,417,978; 5,462,854; 5,469,854; 5,512,295; 5,527,528; 5,534,259; 5,543,152; 5,556,948; 5,580,575; and 5,595,756, each of which is herein incorporated by reference.

[0040] The antisense compounds of the invention encompass any pharmaceutically acceptable salts, esters, or salts of such esters, or any other compound which, upon administration to an animal including a human, is capable of providing (directly or indirectly) the biologically active metabolite or residue thereof. Accordingly, for example, the disclosure is also drawn to prodrugs and pharmaceutically acceptable salts of the compounds of the invention, pharmaceutically acceptable salts of such prodrugs, and other bioequivalents.

[0041] The term "prodrug" indicates a therapeutic agent that is prepared in an inactive form that is converted to an active form (i.e., drug) within the body or cells thereof by the action of endogenous enzymes or other chemicals and/or conditions. In particular, prodrug versions of the oligonucleotides of the invention are prepared as SATE [(S-acetyl-2-thioethyl) phosphate] derivatives according to the methods disclosed in WO 93/24510 to Gosselin et al., published December 9, 1993 or in WO 94/26764 to Imbach et al.

[0042] The term "pharmaceutically acceptable salts" refers to physiologically and pharmaceutically acceptable salts of the compounds of the invention: i.e., salts that retain the desired biological activity of the parent compound and do not impart undesired toxicological effects thereto.

[0043] Pharmaceutically acceptable base addition salts are formed with metals or amines, such as alkali and alkaline earth metals or organic amines. Examples of metals used as cations are sodium, potassium, magnesium, calcium, and the like. Examples of suitable amines are N, N'-dibenzylethylenediamine, chloroprocaine, choline, diethanolamine, dicyclohexylamine, ethylenediamine, N-methylglucamine, and procaine (see, for example, Berge et al., "Pharmaceutical Salts," *J. of Pharma Sci.*, 1977, 66, 119). The base addition salts of said acidic compounds are prepared by contacting the free acid form with a sufficient amount of the desired base to produce the salt in the conventional manner. The free acid form may be

regenerated by contacting the salt form with an acid and isolating the free acid in the conventional manner. The free acid forms differ from their respective salt forms somewhat in certain physical properties such as solubility in polar solvents, but otherwise the salts are equivalent to their respective free acid for purposes of the present invention. As used herein, a "pharmaceutical addition salt" includes a pharmaceutically acceptable salt of an acid form of one of the components of the compositions of the invention. These include organic or inorganic acid salts of the amines. Preferred acid salts are the hydrochlorides, acetates, salicylates, nitrates, and phosphates. Other suitable pharmaceutically acceptable salts are well known to those skilled in the art and include basic salts of a variety of inorganic and organic acids, such as, for example, with inorganic acids, such as for example hydrochloric acid, hydrobromic acid, sulfuric acid or phosphoric acid; with organic carboxylic, sulfonic, sulfo or phospho acids or N-substituted sulfamic acids, for example acetic acid, propionic acid, glycolic acid, succinic acid, maleic acid, hydroxymaleic acid, methylmaleic acid, fumaric acid, malic acid, tartaric acid, lactic acid, oxalic acid, gluconic acid, glucaric acid, glucuronic acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, salicylic acid, 4-aminosalicylic acid, 2-phenoxybenzoic acid, 2-acetoxybenzoic acid, embonic acid, nicotinic acid or isonicotinic acid; and with amino acids, such as the 20 alpha-amino acids involved in the synthesis of proteins in nature, for example glutamic acid or aspartic acid, and also with phenylacetic acid, methanesulfonic acid, ethanesulfonic acid, 2-hydroxyethanesulfonic acid, ethane-1,2-disulfonic acid, benzenesulfonic acid, 4-methylbenzenesulfoic acid, naphthalene-2-sulfonic acid, naphthalene-1,5-disulfonic acid, 2- or 3-phosphoglycerate, glucose-6-phosphate, N-cyclohexylsulfamic acid (with the formation of cyclamates), or with other acid organic compounds, such as ascorbic acid. Pharmaceutically acceptable salts of compounds may also be prepared with a pharmaceutically acceptable cation. Suitable pharmaceutically acceptable cations are well known to those skilled in the art and include alkaline, alkaline earth, ammonium, and quaternary ammonium cations. Carbonates or hydrogen carbonates are also possible.

[0044] For oligonucleotides, preferred examples of pharmaceutically acceptable salts include but are not limited to (a) salts formed with cations such

as sodium, potassium, ammonium, magnesium, calcium, polyamines such as spermine and spermidine, etc.; (b) acid addition salts formed with inorganic acids, for example hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, nitric acid and the like; (c) salts formed with organic acids such as, for example, acetic acid, oxalic acid, tartaric acid, succinic acid, maleic acid, fumaric acid, gluconic acid, citric acid, malic acid, ascorbic acid, benzoic acid, tannic acid, palmitic acid, alginic acid, polyglutamic acid, naphthalenesulfonic acid, methanesulfonic acid, p-toluenesulfonic acid, naphthalenedisulfonic acid, polygalacturonic acid, and the like; and (d) salts formed from elemental anions such as chlorine, bromine, and iodine.

[0045] The antisense compounds of the present invention can be utilized for diagnostics, therapeutics, prophylaxis, and as research reagents and kits. For therapeutics, an animal, preferably a human, suspected of having a disease or disorder, which can be treated by modulating the expression of mPGES-1, is treated by administering antisense compounds in accordance with this invention. The compounds of the invention can be utilized in pharmaceutical compositions by adding an effective amount of an antisense compound to a suitable pharmaceutically acceptable diluent or carrier. Use of the antisense compounds and methods of the invention may also be useful prophylactically, e.g., to prevent or delay infection, inflammation, or tumor formation, for example.

[0046] The antisense compounds of the invention are useful for research and diagnostics, because these compounds hybridize to nucleic acids encoding mPGES-1, enabling sandwich and other assays to easily be constructed to exploit this fact. Hybridization of the antisense oligonucleotides of the invention with a nucleic acid encoding mPGES-1 can be detected by means known in the art. Such means may include conjugation of an enzyme to the oligonucleotide, radiolabelling of the oligonucleotide or any other suitable detection means. Kits using such detection means for detecting the level of mPGES-1 in a sample may also be prepared.

[0047] The present invention also includes pharmaceutical compositions and formulations, which include the antisense compounds of the invention. The pharmaceutical compositions of the present invention may be administered in a

number of ways depending upon whether local or systemic treatment is desired and upon the area to be treated. Administration may be topical (including ophthalmic and to mucous membranes including vaginal and rectal delivery), pulmonary, e.g., by inhalation or insufflation of powders or aerosols, including by nebulizer; intratracheal, intranasal, epidermal and transdermal), oral or parenteral. Parenteral administration includes intravenous, intraarterial, subcutaneous, intraperitoneal or intramuscular injection or infusion; or intracranial, e.g., intrathecal or intraventricular, administration. Oligonucleotides with at least one 2'-O-methoxyethyl modification are believed to be particularly useful for oral administration.

[0048] Pharmaceutical compositions and formulations for topical administration may include transdermal patches, ointments, lotions, creams, gels, drops, suppositories, sprays, liquids, and powders. Conventional pharmaceutical carriers, aqueous, powder or oily bases, thickeners and the like may be necessary or desirable. Coated condoms, gloves, and the like may also be useful.

[0049] Compositions and formulations for oral administration include powders or granules, suspensions, or solutions in water or non-aqueous media, capsules, sachets, or tablets. Thickeners, flavoring agents, diluents, emulsifiers, dispersing aids, or binders may be desirable.

[0050] Compositions and formulations for parenteral, intrathecal or intraventricular administration may include sterile aqueous solutions, which may also contain buffers, diluents and other suitable additives such as, but not limited to, penetration enhancers, carrier compounds and other pharmaceutically acceptable carriers or excipients.

[0051] Pharmaceutical compositions of the present invention include, but are not limited to, solutions, emulsions, and liposome-containing formulations. These compositions may be generated from a variety of components that include, but are not limited to, preformed liquids, self-emulsifying solids and self-emulsifying semisolids.

[0052] The pharmaceutical formulations of the present invention, which may conveniently be presented in unit dosage form, may be prepared according to conventional techniques well known in the pharmaceutical industry. Such

techniques include the step of bringing into association the active ingredients with the pharmaceutical carrier(s) or excipient(s). In general the formulations are prepared by uniformly and intimately bringing into association the active ingredients with liquid carriers or finely divided solid carriers or both, and then, if necessary, shaping the product.

[0053] The compositions of the present invention may be formulated into any of many possible dosage forms such as, but not limited to, tablets, capsules, liquid syrups, soft gels, suppositories, and enemas. The compositions of the present invention may also be formulated as suspensions in aqueous, non-aqueous or mixed media. Aqueous suspensions may further contain substances, which increase the viscosity of the suspension including, for example, sodium carboxymethylcellulose, sorbitol, and/or dextran. The suspension may also contain stabilizers.

[0054] In one embodiment of the present invention the pharmaceutical compositions may be formulated and used as foams. Pharmaceutical foams include formulations such as, but not limited to, emulsions, microemulsions, creams, jellies, and liposomes. While basically similar in nature these formulations vary in the components and the consistency of the final product. The preparation of such compositions and formulations is generally known to those skilled in the pharmaceutical and formulation arts and may be applied to the formulation of the compositions of the present invention. Emulsions

[0055] The compositions of the present invention may be prepared and formulated as emulsions. Emulsions are typically heterogenous systems of one liquid dispersed in another in the form of droplets usually exceeding 0.1 μm in diameter. (Idson, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199; Rosoff, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., Volume 1, p. 245; Block in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 2, p. 335; Higuchi et al., in *Remington's Pharmaceutical Sciences*, Mack Publishing Co., Easton, PA, 1985, p. 301). Emulsions are often biphasic systems comprising of two immiscible liquid phases intimately mixed and dispersed with each other. In general,

emulsions may be either water-in-oil (w/o) or of the oil-in-water (o/w) variety. When an aqueous phase is finely divided into and dispersed as minute droplets into a bulk oily phase the resulting composition is called a water-in-oil (w/o) emulsion. Alternatively, when an oily phase is finely divided into and dispersed as minute droplets into a bulk aqueous phase the resulting composition is called an oil-in-water (o/w) emulsion. Emulsions may contain additional components in addition to the dispersed phases and the active drug, which may be present as a solution in either the aqueous phase, oily phase or itself as a separate phase. Pharmaceutical excipients such as emulsifiers, stabilizers, dyes, and anti-oxidants may also be present in emulsions as needed. Pharmaceutical emulsions may also be multiple emulsions that are comprised of more than two phases such as, for example, in the case of oil-in-water-in-oil (o/w/o) and water-in-oil-in-water (w/o/w) emulsions. Such complex formulations often provide certain advantages that simple binary emulsions do not. Multiple emulsions in which individual oil droplets of an o/w emulsion enclose small water droplets constitute a w/o/w emulsion. Likewise a system of oil droplets enclosed in globules of water stabilized in an oily continuous provides an o/w/o emulsion.

[0056] Emulsions are characterized by little or no thermodynamic stability. Often, the dispersed or discontinuous phase of the emulsion is well dispersed into the external or continuous phase and maintained in this form through the means of emulsifiers or the viscosity of the formulation. Either of the phases of the emulsion may be a semisolid or a solid, as is the case of emulsion-style ointment bases and creams. Other means of stabilizing emulsions entail the use of emulsifiers that may be incorporated into either phase of the emulsion. Emulsifiers may broadly be classified into four categories: synthetic surfactants, naturally occurring emulsifiers, absorption bases, and finely dispersed solids (Idson, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199).

[0057] Synthetic surfactants, also known as surface active agents, have found wide applicability in the formulation of emulsions and have been reviewed in the literature (Rieger, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 285; Idson, in *Pharmaceutical Dosage Forms*, Lieberman,

Rieger and Banker (Eds.), Marcel Dekker, Inc., New York, N.Y., 1988, volume 1, p. 199). Surfactants are typically amphiphilic and comprise a hydrophilic and a hydrophobic portion. The ratio of the hydrophilic to the hydrophobic nature of the surfactant has been termed the hydrophile/lipophile balance (HLB) and is a valuable tool in categorizing and selecting surfactants in the preparation of formulations. Surfactants may be classified into different classes based on the nature of the hydrophilic group: nonionic, anionic, cationic, and amphoteric (Rieger, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 285).

[0058] Naturally occurring emulsifiers used in emulsion formulations include lanolin, beeswax, phosphatides, lecithin, and acacia. Absorption bases possess hydrophilic properties such that they can soak up water to form w/o emulsions yet retain their semisolid consistencies, such as anhydrous lanolin and hydrophilic petrolatum. Finely divided solids have also been used as good emulsifiers especially in combination with surfactants and in viscous preparations. These include polar inorganic solids, such as heavy metal hydroxides, nonswelling clays such as bentonite, attapulgite, hectorite, kaolin, montmorillonite, colloidal aluminum silicate and colloidal magnesium aluminum silicate, pigments and nonpolar solids such as carbon or glyceryl tristearate.

[0059] A large variety of non-emulsifying materials are also included in emulsion formulations and contribute to the properties of emulsions. These include fats, oils, waxes, fatty acids, fatty alcohols, fatty esters, humectants, hydrophilic colloids, preservatives, and antioxidants (Block, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 335; Idson, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199).

[0060] Hydrophilic colloids or hydrocolloids include naturally occurring gums and synthetic polymers such as polysaccharides (for example, acacia, agar, alginic acid, carrageenan, guar gum, karaya gum, and tragacanth), cellulose derivatives (for example, carboxymethylcellulose and carboxypropylcellulose), and synthetic polymers (for example, carbomers,

cellulose ethers, and carboxyvinyl polymers). These disperse or swell in water to form colloidal solutions that stabilize emulsions by forming strong interfacial films around the dispersed phase droplets and by increasing the viscosity of the external phase.

[0061] Since emulsions often contain a number of ingredients such as carbohydrates, proteins, sterols, and phosphatides that may readily support the growth of microbes, these formulations often incorporate preservatives. Commonly used preservatives included in emulsion formulations include methyl paraben, propyl paraben, quaternary ammonium salts, benzalkonium chloride, esters of p-hydroxybenzoic acid, and boric acid. Antioxidants are also commonly added to emulsion formulations to prevent deterioration of the formulation. Antioxidants used may be free radical scavengers such as tocopherols, alkyl gallates, butylated hydroxyanisole, butylated hydroxytoluene, or reducing agents such as ascorbic acid and sodium metabisulfite, and antioxidant synergists such as citric acid, tartaric acid, and lecithin.

[0062] The application of emulsion formulations via dermatological, oral, and parenteral routes and methods for their manufacture have been reviewed in the literature (Idson, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199). Emulsion formulations for oral delivery have been very widely used because of reasons of ease of formulation, efficacy from an absorption and bioavailability standpoint. (Rosoff, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 245; Idson, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199). Mineral-oil base laxatives, oil-soluble vitamins, and high fat nutritive preparations are among the materials that have commonly been administered orally as o/w emulsions.

[0063] In one embodiment of the present invention, the compositions of oligonucleotides and nucleic acids are formulated as microemulsions. A microemulsion may be defined as a system of water, oil, and amphiphile, which is a single optically isotropic, and thermodynamically stable liquid solution (Rosoff, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker

(Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 245). Typically microemulsions are systems that are prepared by first dispersing an oil in an aqueous surfactant solution and then adding a sufficient amount of a fourth component, generally an intermediate chain-length alcohol to form a transparent system. Therefore, microemulsions have also been described as thermodynamically stable, isotropically clear dispersions of two immiscible liquids that are stabilized by interfacial films of surface-active molecules (Leung and Shah, in: *Controlled Release of Drugs: Polymers and Aggregate Systems*, Rosoff, M., Ed., 1989, VCH Publishers, New York, pages 1852-5). Microemulsions commonly are prepared via a combination of three to five components that include oil, water, surfactant, cosurfactant, and electrolyte. Whether the microemulsion is of the water-in-oil (w/o) or an oil-in-water (o/w) type is dependent on the properties of the oil and surfactant used and on the structure and geometric packing of the polar heads and hydrocarbon tails of the surfactant molecules (Schott, in *Remington's Pharmaceutical Sciences*, Mack Publishing Co., Easton, PA, 1985, p. 271).

[0064] The phenomenological approach utilizing phase diagrams has been extensively studied and has yielded a comprehensive knowledge, to one skilled in the art, of how to formulate microemulsions (Rosoff, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 245; Block, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 335). Compared to conventional emulsions, microemulsions offer the advantage of solubilizing water-insoluble drugs in a formulation of thermodynamically stable droplets that are formed spontaneously.

[0065] Surfactants used in the preparation of microemulsions include, but are not limited to, ionic surfactants, non-ionic surfactants, Brij 96, polyoxyethylene oleyl ethers, polyglycerol fatty acid esters, tetraglycerol monolaurate (ML310), tetraglycerol monooleate (MO310), hexaglycerol monooleate (PO310), hexaglycerol pentaoleate (PO500), decaglycerol monocaprate (MCA750), decaglycerol monooleate (MO750), decaglycerol sequioleate (S0750), decaglycerol decaoleate (DAO750), alone or in

combination with cosurfactants. The cosurfactant, usually a short-chain alcohol such as ethanol, 1-propanol, and 1-butanol, serves to increase the interfacial fluidity by penetrating into the surfactant film and consequently creating a disordered film because of the void space generated among surfactant molecules. Microemulsions may, however, be prepared without the use of cosurfactants and alcohol-free self-emulsifying microemulsion systems are known in the art. The aqueous phase may typically be, but is not limited to, water, an aqueous solution of the drug, glycerol, PEG300, PEG400, polyglycerols, propylene glycols, and derivatives of ethylene glycol. The oil phase may include, but is not limited to, materials such as Captex 300, Captex 355, Capmul MCM, fatty acid esters, medium chain (C8-C12) mono, di, and triglycerides, polyoxyethylated glyceryl fatty acid esters, fatty alcohols, polyglycolized glycerides, saturated polyglycolized C8-C10 glycerides, vegetable oils and silicone oil.

[0066] Microemulsions are particularly of interest from the standpoint of drug solubilization and the enhanced absorption of drugs. Lipid based microemulsions (both o/w and w/o) have been proposed to enhance the oral bioavailability of drugs, including peptides (Constantinides et al., *Pharmaceutical Research*, 1994, 11, 1385-1390; Ritschel, *Meth. Find. Exp. Clin. Pharmacol.,* 1993, 13, 205). Microemulsions afford advantages of improved drug solubilization, protection of drug from enzymatic hydrolysis, possible enhancement of drug absorption due to surfactant-induced alterations in membrane fluidity and permeability, ease of preparation, ease of oral administration over solid dosage forms, improved clinical potency, and decreased toxicity (Constantinides et al., *Pharmaceutical Research*, 1994, 11, 1385; Ho et al., *J. Pharm. Sci.*, 1996, 85, 138-143). Often microemulsions may form spontaneously when their components are brought together at ambient temperature. This may be particularly advantageous when formulating thermolabile drugs, peptides, or oligonucleotides. Microemulsions have also been effective in the transdermal delivery of active components in both cosmetic and pharmaceutical applications. It is expected that the microemulsion compositions and formulations of the present invention will facilitate the increased systemic absorption of oligonucleotides and nucleic acids from the

gastrointestinal tract, as well as improve the local cellular uptake of oligonucleotides and nucleic acids within the gastrointestinal tract, vagina, buccal cavity and other areas of administration.

[0067] Microemulsions of the present invention may also contain additional components and additives such as sorbitan monostearate (Grill 3), Labrasol, and penetration enhancers to improve the properties of the formulation and to enhance the absorption of the oligonucleotides and nucleic acids of the present invention. Penetration enhancers used in the microemulsions of the present invention may be classified as belonging to one of five broad categories - surfactants, fatty acids, bile salts, chelating agents, and non-chelating non-surfactants (Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, p. 92). Each of these classes has been discussed above.

Liposomes

[0068] There are many organized surfactant structures besides microemulsions that have been studied and used for the formulation of drugs. These include monolayers, micelles, bilayers, and vesicles. Vesicles, such as liposomes, have attracted great interest because of their specificity and the duration of action they offer from the standpoint of drug delivery. As used in the present invention, the term "liposome" means a vesicle composed of amphiphilic lipids arranged in a spherical bilayer or bilayers.

[0069] Liposomes are unilamellar or multilamellar vesicles which have a membrane formed from a lipophilic material and an aqueous interior. The aqueous portion contains the composition to be delivered. Cationic liposomes possess the advantage of being able to fuse to the cell wall. Noncationic liposomes, although not able to fuse as efficiently with the cell wall, are taken up by macrophages in vivo.

[0070] In order to cross intact mammalian skin, lipid vesicles must pass through a series of fine pores, each with a diameter less than 50 nm, under the influence of a suitable transdermal gradient. Therefore, it is desirable to use a liposome, which is highly deformable and able to pass through such fine pores.

[0071] Further advantages of liposomes include; liposomes obtained from natural phospholipids are biocompatible and biodegradable; liposomes can

incorporate a wide range of water and lipid soluble drugs; liposomes can protect encapsulated drugs in their internal compartments from metabolism and degradation (Rosoff, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, P. 245). Important considerations in the preparation of liposome formulations are the lipid surface charge, vesicle size, and the aqueous volume of the liposomes.

[0072] Liposomes are useful for the transfer and delivery of active ingredients to the site of action. Because the liposomal membrane is structurally similar to biological membranes, when liposomes are applied to a tissue, the liposomes start to merge with the cellular membranes. As the merging of the liposome and cell progresses, the liposomal contents are emptied into the cell where the active agent may act.

[0073] Liposomal formulations have been the focus of extensive investigation as the mode of delivery for many drugs. There is growing evidence that for topical administration, liposomes present several advantages over other formulations. Such advantages include reduced side-effects related to high systemic absorption of the administered drug, increased accumulation of the administered drug at the desired target, and the ability to administer a wide variety of drugs, both hydrophilic and hydrophobic, into the skin.

[0074] Several reports have detailed the ability of liposomes to deliver agents including high-molecular weight DNA into the skin. Compounds including analgesics, antibodies, hormones, and high-molecular weight DNAs have been administered to the skin. The majority of applications resulted in the targeting of the upper epidermis.

[0075] Liposomes fall into two broad classes. Cationic liposomes are positively charged liposomes, which interact with the negatively charged DNA molecules to form a stable complex. The positively charged DNA/liposome complex binds to the negatively charged cell surface and is internalized in an endosome. Due to the acidic pH within the endosome, the liposomes are ruptured, releasing their contents into the cell cytoplasm (Wang et al., *Biochem. Biophys. Res. Commun.*, 1987, 147, 980 - 985)

[0076] Liposomes, which are pH-sensitive or negatively charged, entrap DNA rather than complex with it. Since both the DNA and the lipid are

similarly charged, repulsion rather than complex formation occurs. Nevertheless, some DNA is entrapped within the aqueous interior of these liposomes. pH-sensitive liposomes have been used to deliver DNA encoding the thymidine kinase gene to cell monolayers in culture. Expression of the exogenous gene was detected in the target cells (Zhou et al., *Journal of Controlled Release*, 1992, 19, 269-274).

[0077] One major type of liposomal composition includes phospholipids other than naturally derived phosphatidylcholine. Neutral liposome compositions, for example, can be formed from dimyristoyl phosphatidylcholine (DMPC) or dipalmitoyl phosphatidylcholine (DPPC). Anionic liposome compositions generally are formed from dimyristoyl phosphatidylglycerol, while anionic fusogenic liposomes are formed primarily from dioleoyl phosphatidylethanolamine (DOPE). Another type of liposomal composition is formed from phosphatidylcholine (PC) such as, for example, soybean PC, and egg PC. Another type is formed from mixtures of phospholipid and/or phosphatidylcholine and/or cholesterol.

[0078] Several studies have assessed the topical delivery of liposomal drug formulations to the skin. Application of liposomes containing interferon to guinea pig skin resulted in a reduction of skin herpes sores while delivery of interferon via other means (e.g. as a solution or as an emulsion) were ineffective (Weiner et al., *Journal of Drug Targeting*, 1992, 2, 405-410). Further, an additional study tested the efficacy of interferon administered as part of a liposomal formulation to the administration of interferon using an aqueous system, and concluded that the liposomal formulation was superior to aqueous administration (du Plessis et al., *Antiviral Research*, 1992, 18, 259-265).

[0079] Non-ionic liposomal systems have also been examined to determine their utility in the delivery of drugs to the skin, in particular systems comprising non-ionic surfactant and cholesterol. Non-ionic liposomal formulations comprising Novasome ™ I (glyceryl dilaurate/cholesterol/polyoxyethylene-10-stearyl ether) and Novasome™ II (glyceryl distearate/ cholesterol/polyoxyethylene-10-stearyl ether) were used to deliver cyclosporin-A into the dermis of mouse skin. Results indicated that such non-ionic

liposomal systems were effective in facilitating the deposition of cyclosporin-A into different layers of the skin (Hu et al. *S.T.P.Pharma. Sci.*, 1994, 4, 6, 466).

[0080] Liposomes also include "sterically stabilized" liposomes, a term that, as used herein, refers to liposomes comprising one or more specialized lipids that, when incorporated into liposomes, result in enhanced circulation lifetimes relative to liposomes lacking such specialized lipids. Examples of sterically stabilized liposomes are those in which part of the vesicle-forming lipid portion of the liposome (A) comprises one or more glycolipids, such as monosialoganglioside G_{M1}, or (B) is derivatized with one or more hydrophilic polymers, such as a polyethylene glycol (PEG) moiety. While not wishing to be bound by any particular theory, it is thought in the art that, at least for sterically stabilized liposomes containing gangliosides, sphingomyelin, or PEG-derivatized lipids, the enhanced circulation half-life of these sterically stabilized liposomes derives from a reduced uptake into cells of the reticuloendothelial system (RES) (Allen et al., *FEBS Letters*, 1987, 223, 42; Wu et al., *Cancer Research*, 1993, 53, 3765).

[0081] Various liposomes comprising one or more glycolipids are known in the art. Papahadjopoulos et al. (*Ann. N.Y. Acad. Sci.*, 1987, 507, 64) reported the ability of monosialoganglioside G_{M1}, galactocerebroside sulfate and phosphatidylinositol to improve blood half-lives of liposomes. These findings were expounded upon by Gabizon et al. (*Proc. Natl. Acad. Sci. U.S.A.*, 1988, 85, 6949). U.S. Patent No. 4,837,028 and WO 88/04924, both to Allen et al., disclose liposomes comprising (1) sphingomyelin and (2) the ganglioside Gjor a galactocerebroside sulfate ester. U.S. Patent No. 5,543,152 (Webb et al.) discloses liposomes comprising sphingomyelin. Liposomes comprising 1,2-sn-dimyristoylphosphatidylcholine are disclosed in WO 97/13499 (Lim et al.).

[0082] Many liposomes comprising lipids derivatized with one or more hydrophilic polymers, and methods of preparation thereof, are known in the art. Sunamoto et al. (*Bull. Chem. Soc. Jpn.*, 1980, 53, 2778) described liposomes comprising a nonionic detergent, $2C_{12}15G$, which contains a PEG moiety. Illum et al. (*FEBS Lett.*, 1984, 167, 79) noted that hydrophilic coating of polystyrene particles with polymeric glycols results in significantly enhanced blood half-lives. Synthetic phospholipids modified by the attachment of carboxylic groups

of polyalkylene glycols (e.g., PEG) are described by Sears (U.S. Patent Nos. 4,426,330 and 4,534,899). Klibanov et al. (*FEBS Lett.*, 1990, 268, 235) described experiments demonstrating that liposomes comprising phosphatidylethanolamine (PE) derivatized with PEG or PEG stearate have significant increases in blood circulation half-lives. Blume et al. (*Biochimica et Biophysica Acta*, 1990, 1029, 91) extended such observations to other PEG derivatized phospholipids, e.g., DSPE-PEG, formed from the combination of distearoylphosphatidylethanolamine (DSPE) and PEG. Liposomes having covalently bound PEG moieties on their external surface are described in European Patent No. EP 0 445 131 B1 and WO 90/04384 to Fisher. Liposome compositions containing 1-20 mole percent of PE derivatized with PEG, and methods of use thereof, are described by Woodle et al. (U.S. Patent Nos. 5,013,556 and 5,356,633) and Martin et al. (U.S. Patent No. 5,213,804 and European Patent No. EP 0 496 813 Bl). Liposomes comprising a number of other lipid-polymer conjugates are disclosed in WO 91/05545 and U.S. Patent No. 5,225,212 (both to Martin et al.) and in WO 94/20073 (Zalipsky et al.) Liposomes comprising PEG-modified ceramide lipids are described in WO 96/10391 (Choi et al.). U.S. Patent Nos. 5,540,935 (Miyazaki et al.) and 5,556,948 (Tagawa et al.) describe PEG-containing liposomes that can be further derivatized with functional moieties on their surfaces.

[0083] A limited number of liposomes comprising nucleic acids are known in the art. WO 96/40062 to Thierry et al. discloses methods for encapsulating high molecular weight nucleic acids in liposomes. U.S. Patent No. 5,264,221 to Tagawa et al. discloses protein-bonded liposomes and asserts that the contents of such liposomes may include an antisense RNA. U.S. Patent No. 5,665,710 to Rahman et al. describes certain methods of encapsulating oligodeoxynucleotides in liposomes. WO 97/04787 to Love et al. discloses liposomes comprising antisense oligonucleotides targeted to the raf gene.

[0084] Transfersomes are yet another type of liposomes, and are highly deformable lipid aggregates which are attractive candidates for drug delivery vehicles. Transfersomes may be described as lipid droplets, which are so highly deformable that they are easily able to penetrate through pores that are smaller than the droplet. Transfersomes are adaptable to the environment in which they

are used, e.g. they are self-optimizing (adaptive to the shape of pores in the skin), self-repairing, frequently reach their targets without fragmenting, and often self-loading. To make transfersomes it is possible to add surface edge-activators, usually surfactants, to a standard liposomal composition.

Transfersomes have been used to deliver serum albumin to the skin. The transfersome-mediated delivery of serum albumin has been shown to be as effective as subcutaneous injection of a solution containing serum albumin.

[0085] Surfactants find wide application in formulations such as emulsions (including microemulsions) and liposomes. The most common way of classifying and ranking the properties of the many different types of surfactants, both natural and synthetic, is by the use of the hydrophile/lipophile balance (HLB). The nature of the hydrophilic group (also known as the "head") provides the most useful means for categorizing the different surfactants used in formulations (Rieger, in *Pharmaceutical Dosage Forms*, Marcel Dekker, Inc., New York, NY, 1988, p. 285)

[0086] If the surfactant molecule is not ionized, it is classified as a nonionic surfactant. Nonionic surfactants find wide application in pharmaceutical and cosmetic products and are usable over a wide range of pH values. In general their HLB values range from 2 to about 18 depending on their structure. Nonionic surfactants include nonionic esters such as ethylene glycol esters, propylene glycol esters, glyceryl esters, polyglyceryl esters, sorbitan esters, sucrose esters, and ethoxylated esters. Nonionic alkanolamides and ethers such as fatty alcohol ethoxylates, propoxylated alcohols, and ethoxylated/propoxylated block polymers are also included in this class. The polyoxyethylene surfactants are the most popular members of the nonionic surfactant class.

[0087] If the surfactant molecule carries a negative charge when it is dissolved or dispersed in water, the surfactant is classified as anionic. Anionic surfactants include carboxylates such as soaps, acyl lactylates, acyl amides of amino acids, esters of sulfuric acid such as alkyl sulfates and ethoxylated alkyl sulfates, sulfonates such as alkyl benzene sulfonates, acyl isethionates, acyl taurates and sulfosuccinates, and phosphates. The most important members of the anionic surfactant class are the alkyl sulfates and the soaps.

[0088] If the surfactant molecule carries a positive charge when it is dissolved or dispersed in water, the surfactant is classified as cationic. Cationic surfactants include quaternary ammonium salts and ethoxylated amines. The quaternary ammonium salts are the most used members of this class.

[0089] If the surfactant molecule has the ability to carry either a positive or negative charge, the surfactant is classified as amphoteric. Amphoteric surfactants include acrylic acid derivatives, substituted alkylamides, N-alkylbetaines, and phosphatides.

[0090] The use of surfactants in drug products, formulations and in emulsions has been reviewed (Rieger, in *Pharmaceutical Dosage Forms*, Marcel Dekker, Inc., New York, NY, 1988, p. 285). Penetration Enhancers

[0091] In one embodiment, the present invention employs various penetration enhancers to effect the efficient delivery of nucleic acids particularly oligonucleotides, to the skin of animals. Most drugs are present in solution in both ionized and nonionized forms. However, usually only lipid soluble or lipophilic drugs readily cross cell membranes. It has been discovered that even non-lipophilic drugs may cross cell membranes if the membrane to be crossed is treated with a penetration enhancer. In addition to aiding the diffusion of non-lipophilic drugs across cell membranes, penetration enhancers also enhance the permeability of lipophilic drugs.

[0092] Penetration enhancers may be classified as belonging to one of five broad categories, i.e., surfactants, fatty acids, bile salts, chelating agents, and non-chelating nonsurfactants (Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, p.92). Each of the above mentioned classes of penetration enhancers are described below in greater detail.

[0093] Surfactants: In connection with the present invention, surfactants (or "surface-active agents") are chemical entities which, when dissolved in an aqueous solution, reduce the surface tension of the solution or the interfacial tension between the aqueous solution and another liquid, with the result that absorption of oligonucleotides through the mucosa. is enhanced. In addition to bile salts and fatty acids, these penetration enhancers include, for example, sodium lauryl sulfate, polyoxyethylene-9-lauryl ether and polyoxyethylene-20-cetyl ether) (Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*,

1991, p.92); and perfluorochemical emulsions, such as FC-43. Takahashi et al., *J. Pharm. Pharmacol.*, 1988, 40, 252).

[0094] Fatty acids: Various fatty acids and their derivatives which act as penetration enhancers include, for example, oleic acid, lauric acid, capric acid (n-decanoic acid), myristic acid, palmitic acid, stearic acid, linoleic acid, linolenic acid, dicaprate, tricaprate, monoolein (1-monooleoyl-.rac-glycerol), dilaurin, caprylic acid, arachidonic acid, glycerol 1-monocaprate, 1-dodecylazacycloheptan-2-one, acylcarnitines, acylcholines, C_{1-10} alkyl esters thereof (e.g., methyl, isopropyl and t-butyl), and mono- and di-glycerides thereof (i.e., oleate, laurate, caprate, myristate, palmitate, stearate, linoleate, etc.) (Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, p.92; Muranishi, *Critical Reviews in Therapeutic Drug Carrier Systems*, 1990, 7, 1-33; El Hariri et al., *J. Pharm. Pharmacol.*, 1992, 44, 651-654).

[0095] Bile salts: The physiological role of bile includes the facilitation of dispersion and absorption of lipids and fat-soluble vitamins (Brunton, Chapter 38 in: Goodman & Gilman's *The Pharmacological Basis of Therapeutics*, 9th Ed., Hardman et al. Eds. McGraw-Hill, New York, 1996, pp. 934-935). Various natural bile salts, and their synthetic derivatives, act as penetration enhancers. Thus the term "bile salts" includes any of the naturally occurring components of bile as well as any of their synthetic derivatives. The bile salts of the invention include, for example, cholic acid (or its pharmaceutically acceptable sodium salt, sodium cholate), dehydrocholic acid (sodium dehydrocholate), deoxycholic acid (sodium deoxycholate), glucholic acid (sodium glucholate), glycholic acid (sodium glycocholate), glycodeoxycholic acid (sodium glycodeoxycholate), taurocholic acid (sodium taurocholate), taurodeoxycholic acid (sodium taurodeoxycholate), chenodeoxycholic acid (sodium chenodeoxycholate), ursodeoxycholic acid (UDCA), sodium tauro-24,25-dihydro-fusidate (STDHF), sodium glycodihydrofusidate and polyoxyethylene-9-lauryl ether (POE) (Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, page 92; Swinyard, Chapter 39 In: *Remington's Pharmaceutical Sciences*, 18th Ed., Gennaro, ed., Mack Publishing Co., Easton, PA, 1990, pages 782-783; Muranishi, *Critical Reviews in Therapeutic Drug Carrier Systems*, 1990, 7, 1-

33; Yamamoto et al., *J. Pharm. Exp. Ther.*, 1992, 263, 25; Yamashita et al., *J. Pharm. Sci.*, 1990, 79, 579-583).

[0096] Chelating Agents: Chelating agents, as used in connection with the present invention, can be defined as compounds that remove metallic ions from solution by forming complexes therewith, with the result that absorption of oligonucleotides through the mucosa is enhanced. With regards to their use as penetration enhancers in the present invention, chelating agents have the added advantage of also serving as DNase inhibitors, as most characterized DNA nucleases require a divalent metal ion for catalysis and are thus inhibited by chelating agents (Jarrett, *J. Chromatogr.*, 1993, 618, 315-339). Chelating agents of the invention include but are not limited to disodium. ethylenediaminetetraacetate (EDTA), citric acid, salicylates (e.g., sodium salicylate, 5-methoxysalicylate and homovanilate), N-acyl derivatives of collagen, laureth-9, and N-amino acyl derivatives of beta-diketones (enamines)(Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, page 92; Muranishi, *Critical Reviews in Therapeutic Drug Carrier Systems*, 1990, 7, 1-33; Buur et al., *J. Control Rel.*, 1990, 14, 43-51).

[0097] Non-chelating non-surfactants: As used herein, nonchelating non-surfactant penetration enhancing compounds can be defined as compounds that demonstrate insignificant activity as chelating agents or as surfactants but that nonetheless enhance absorption of oligonucleotides through the alimentary mucosa (Muranishi, *Critical Reviews in Therapeutic Drug Carrier Systems*, 1990, 7, 1-33). This class of penetration enhancers include, for example, unsaturated cyclic ureas, 1-alkyl- and 1-alkenylazacyclo-alkanone derivatives (Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, page 92); and non-steroidal anti-inflammatory agents such as diclofenac sodium, indomethacin and phenylbutazone (Yamashita et al., *J. Pharm. Pharmacol.*, 1987, 39, 621-626).

[0098] Agents that enhance uptake of oligonucleotides at the cellular level may also be added to the pharmaceutical and other compositions of the present invention. For example, cationic lipids, such as lipofectin (Junichi et al, U.S. Patent No. 5,705,188), cationic glycerol derivatives, and polycationic

molecules, such as polylysine (Lollo et al., PCT Application WO 97/30731), are also known to enhance the cellular uptake of oligonucleotides.

[0099] Other agents may be utilized to enhance the penetration of the administered nucleic acids, including glycols such as ethylene glycol and propylene glycol, pyrrols such as 2-pyrrol, azones, and terpenes such as limonene and menthone.

Carriers

[00100] Certain compositions of the present invention also incorporate carrier compounds in the formulation. As used herein, "carrier compound" or "carrier" can refer to a nucleic acid, or analog thereof, which is inert (i.e., does not possess biological activity per se) but is recognized as a nucleic acid by in vivo processes that reduce the bioavailability of a nucleic acid having biological activity by, for example, degrading the biologically active nucleic acid or promoting its removal from circulation. The coadministration of a nucleic acid and a carrier compound, typically with an excess of the latter substance, can result in a substantial reduction of the amount of nucleic acid recovered in the liver, kidney or other extracirculatory reservoirs, presumably due to competition between the carrier compound and the nucleic acid for a common receptor. For example, the recovery of a partially phosphorothioate oligonucleotide in hepatic tissue can be reduced when it is coadministered with polyinosinic acid, dextran sulfate, polycytidic acid or 4-acetamido-4'isothiocyano-stilbene-2,2'disulfonic acid (Miyao et al., *Antisense Res. Dev.*, 1995, 5, 115-121; Takakura et al., *Antisense & Nucl. Acid Drug Dev.*, 1996, 6, 177-183).

Excipients

[00101] In contrast to a carrier compound, a "pharmaceutical carrier" or "excipient" is a pharmaceutically acceptable solvent, suspending agent or any other pharmacologically inert vehicle for delivering one or more nucleic acids to an animal. The excipient may be liquid or solid and is selected, with the planned manner of administration in mind, so as to provide for the desired bulk, consistency, etc., when combined with a nucleic acid and the other components of a given pharmaceutical composition. Typical pharmaceutical carriers include,

but are not limited to, binding agents (e.g., pregelatinized maize starch, polyvinylpyrrolidone or hydroxypropyl methylcellulose, etc.); fillers (e.g., lactose and other sugars, microcrystalline cellulose, pectin, gelatin, calcium sulfate, ethyl cellulose, polyacrylates or calcium hydrogen phosphate, etc.); lubricants (e.g., magnesium stearate, talc, silica, colloidal silicon dioxide, stearic acid, metallic stearates, hydrogenated vegetable oils, corn starch, polyethylene glycols, sodium benzoate, sodium acetate, etc.); disintegrants (e.g., starch, sodium starch glycolate, etc.); and wetting agents (e.g., sodium lauryl sulphate, etc.).

[00102] Pharmaceutically acceptable organic or inorganic excipient suitable for non-parenteral administration which do not deleteriously react with nucleic acids can also be used to formulate the compositions of the present invention. Suitable pharmaceutically acceptable carriers include, but are not limited to, water, salt solutions, alcohols, polyethylene glycols, gelatin, lactose, amylose, magnesium stearate, talc, silicic acid, viscous paraffin, hydroxymethylcellulose, polyvinylpyrrolidone and the like.

[00103] Formulations for topical administration of nucleic acids may include sterile and non-sterile aqueous solutions, non-aqueous solutions in common solvents such as alcohols, or solutions of the nucleic acids in liquid or solid oil bases. The solutions may also contain buffers, diluents, and other suitable additives. Pharmaceutically acceptable organic or inorganic excipients suitable for non-parenteral administration, which do not deleteriously react with nucleic acids, can be used.

[00104] Suitable pharmaceutically acceptable excipients include, but are not limited to, water, salt solutions, alcohol, polyethylene glycols, gelatin, lactose, amylose, magnesium stearate, talc, silicic acid, viscous paraffin, hydroxymethylcellulose, polyvinylpyrrolidone and the like.

Other Components

[00105] The compositions of the present invention may additionally contain other adjunct components conventionally found in pharmaceutical compositions, at their art-established usage levels. Thus, for example, the compositions may contain additional, compatible, pharmaceutically-active

materials such as, for example, antipruritics, astringents, local anesthetics or anti-inflammatory agents, or may contain additional materials useful in physically formulating various dosage forms of the compositions of the present invention, such as dyes, flavoring agents, preservatives, antioxidants, opacifiers, thickening agents and stabilizers. However, such materials, when added, should not unduly interfere with the biological activities of the components of the compositions of the present invention.' The formulations can be sterilized and, if desired, mixed with auxiliary agents, e.g., lubricants, preservatives, stabilizers, wetting agents, emulsifiers, salts for influencing osmotic pressure, buffers, colorings, flavorings and/or aromatic substances and the like which do not deleteriously interact with the nucleic acid(s) of the formulation.

[00106] Aqueous suspensions may contain substances, which increase the viscosity of the suspension including, for example, sodium carboxymethylcellulose, sorbitol, and/or dextran. The suspension may also contain stabilizers.

[00107] Certain embodiments of the invention provide pharmaceutical compositions containing (a) one or more antisense compounds and (b) one or more other chemotherapeutic agents which function by a non-antisense mechanism. Examples of such chemotherapeutic agents include, but are not limited to, anticancer drugs such as daunorubicin, dactinomycin, doxorubicin, bleomycin, mitomycin, nitrogen mustard, chlorambucil, melphalan, cyclophosphamide, 6-mercaptopurine, 6-thioguanine, cytarabine (CA), 5-fluorouracil (5-FU), floxuridine (5-FUdR), methotrexate (MTX), colchicine, vincristine, vinblastine, etoposide, teniposide, cisplatin and diethylstilbestrol (DES). See, generally, *The Merck Manual of Diagnosis and Therapy*, 15th Ed., Berkow et al., eds., 1987, Rahway, N.J., pages 1206-1228). Anti-inflammatory drugs, including but not limited to nonsteroidal anti-inflammatory drugs and corticosteroids, and antiviral drugs, including but not limited to ribivirin, vidarabine, acyclovir and ganciclovir, may also be combined in compositions of the invention. See, generally, *The Merck Manual of Diagnosis and Therapy*, 15th Ed., Berkow et al., eds., 1987, Rahway, N.J., pages 2499-2506 and 46-49, respectively). other non-antisense chemotherapeutic agents are also within the

scope of this invention. Two or more combined compounds may be used together or sequentially.

[00108] In another related embodiment, compositions of the invention may contain one or more antisense compounds, particularly oligonucleotides, targeted to a first nucleic acid and one or more additional antisense compounds targeted to a second nucleic acid target. Numerous examples of antisense compounds are known in the art. Two or more combined compounds may be used together or sequentially.

[00109] The formulation of therapeutic compositions and their subsequent administration is believed to be within the skill of those in the art. Dosing is dependent on severity and responsiveness of the disease state to be treated, with the course of treatment lasting from several days to several months, or until a cure is effected or a diminution of the disease state is achieved. Optimal dosing schedules can be calculated from measurements of drug accumulation in the body of the patient. Persons of ordinary skill can easily determine optimum dosages, dosing methodologies and repetition rates. Optimum dosages may vary depending on the relative potency of individual oligonucleotides, and can generally be estimated based on EC_{50}s found to be effective in in vitro and in vivo animal models. In general, dosage is from 0.01 µg to 100 g per kg of body weight, and may be given once or more daily, weekly, monthly or yearly, or even once every 2 to 20 years. Persons of ordinary skill in the art can easily estimate repetition rates for dosing based on measured residence times and concentrations of the drug in bodily fluids or tissues. Following successful treatment, it may be desirable to have the patient undergo maintenance therapy to prevent the recurrence of the disease state, wherein the oligonucleotide is administered in maintenance doses, ranging from 0.01 µg to 100 g per kg of body weight, once or more daily, to once every 20 years.

[00110] While the present invention has been described with specificity in accordance with certain of its preferred embodiments, the following examples serve only to illustrate the invention and are not intended to limit the same.

EXAMPLES

Example 1

Nucleoside Phosphoramidites for Oligonucleotide Synthesis Deoxy and 2'-alkoxy amidites

[00111] 2'-Deoxy and 2'-methoxy beta-cyanoethyldiisopropyl phosphoramidites are available from commercial sources (e.g. Chemgenes, Needham MA or Glen Research, Inc. Sterling VA). Other 2'-O-alkoxy substituted nucleoside amidites are prepared as described in U.S. Patent 5,506,351, herein incorporated by reference. For oligonucleotides synthesized using 2'-alkoxy amidites, the standard cycle for unmodified oligonucleotides is utilized, except the wait step after pulse delivery of tetrazole and base is increased to 360 seconds.

[00112] Oligonucleotides containing 5-methyl-2'-deoxycytidine (5-Me-C) nucleotides are synthesized according to published methods [Sanghvi, et. al., *Nucleic Acids Research*, 1993, 21, 3197-3203] using commercially available phosphoramidites (Glen Research, Sterling VA or ChemGenes, Needham MA).

2'-Fluoro amidites

2'-Fluorodeoxyadenosine amidites

[00113] 2'-fluoro oligonucleotides are synthesized as described previously [Kawasaki, et. al., *J. Med. Chem.*, 1993, 36, 831-841] and United States patent 5,670,633, herein incorporated by reference. Briefly, the protected nucleoside N6-benzoyl-2'-deoxy-2'-fluoroadenosine is synthesized utilizing commercially available 9-beta-D-arabinofuranosyladenine as starting material and by modifying literature procedures whereby the 2'-alpha-fluoro atom is introduced by an S_N2-displacement of a 2'-beta-trityl group. Thus N6-benzoyl-9-beta-D-arabinofuranosyladenine is selectively protected in moderate yield as the 3',5'-ditetrahydropyranyl (THP) intermediate. Deprotection of the THP and N6-benzoyl groups is accomplished using standard methodologies and standard

methods are used to obtain the 5'-dimethoxytrityl-(DMT) and 5'-DMT-3'-phosphoramidite intermediates.

2'-Fluorodeoxyguanosine

[00114] The synthesis of 2'-deoxy-2'-fluoroguanosine is accomplished using tetraisopropyldisiloxanyl (TPDS) protected 9-beta-D-arabinofuranosylguanine as starting material, and conversion to the intermediate diisobutyrylarabinofuranosylguanosine. Deprotection of the TPDS group is followed by protection of the hydroxyl group with THP to give diisobutyryl di-THP protected arabinofuranosylguanine. Selective O-deacylation and triflation is followed by treatment of the crude product with fluoride, then deprotection of the THP groups. Standard methodologies are used to obtain the 5'-DMT- and 5'-DMT-3'-phosphoramidites.

2'-Fluorouridine

[00115] Synthesis of 2'-deoxy-2'-fluorouridine is accomplished by the modification of a literature procedure in which 2,2'anhydro-l-beta-D-arabinofuranosyluracil is treated with 70% hydrogen fluoride-pyridine. Standard procedures are used to obtain the 5'-DMT and 5'-DMT-3'-phosphoramidites.

2'-Fluorodeoxycytidine

[00116] 2'-deoxy-2'-fluorocytidine is synthesized via amination of 2'-deoxy-2'-fluorouridine, followed by selective protection to give N4-benzoyl-2'-deoxy-2'-fluorocytidine. Standard procedures are used to obtain the 5'-DMT and 5'-DMT-3'phosphoramidites.

2'-O-(2-Methoxyethyl) modified amidites

[00117] 2'-O-Methoxyethyl-substituted nucleoside amidites are prepared as follows, or alternatively, as per the methods of Martin, P., *Helvetica Chimica Acta*, 1995, 78, 486-504.

2,2'-Anhydro[l-(beta-D-arabinofuranosyl)-5-methyluridinel

[00118] 5-Methyluridine (ribosylthymine, commercially available through Yamasa, Choshi, Japan) (72.0 g, 0.279 M), diphenylcarbonate (90.0 g, 0.420 M) and sodium bicarbonate (2.0 g, 0.024 M) are added to DMF (300 mL). The mixture is heated to reflux, with stirring, allowing the evolved carbon dioxide gas to be released in a controlled manner. After 1 hour, the slightly darkened solution is concentrated under reduced pressure. The resulting syrup is poured into diethylether (2.5 L), with stirring. The product formed a gum. The ether is decanted and the residue is dissolved in a minimum amount of methanol (ca. 400 mL). The solution is poured into fresh ether (2.5 L) to yield a stiff gum. The ether is decanted and the gum is dried in a vacuum oven (60°C at 1 mm Hg for 24 h) to give a solid that is crushed to a light tan powder. The material is used as is for further reactions (or it can be purified further by column chromatography using a gradient of methanol in ethyl acetate (10-25%) to give a white solid.

2'-O-Methoxyethyl-5-methyluridine

[00119] 2,2'-Anhydro-5-methyluridine (195 g, 0.81 M), tris(2-methoxyethyl)borate (231 g, 0.98 M) and 2-methoxyethanol (1.2 L) are added to a 2 L stainless steel pressure vessel and placed in a pre-heated oil bath at 160°C. After heating for 48 hours at 155-160°C, the vessel is opened and the solution evaporated to dryness and triturated with MeOH (200 mL). The residue is suspended in hot acetone (1 L). The insoluble salts are filtered, washed with acetone (150 mL) and the filtrate evaporated. The residue (280 g) is dissolved in CH_3CN (600 mL) and evaporated. A silica gel column (3 kg) is packed in CH_2Cl_2 /acetone /MeOH (20:5:3) containing 0.5% Et_3NH. The residue is dissolved in CH_2C1_2 (250 mL) and adsorbed onto silica (150 g) prior to loading onto the column. The product is eluted with the packing solvent to give the title product. Additional material can be obtained by reworking impure fractions.

2'-O-Methoxyethyl-5'-O-dimethoxytrityl-5-methyluridine

[00120] 2'-O-Methoxyethyl-5-methyluridine (160 g, 0.506 M) is co-evaporated with pyridine (250 mL) and the dried residue dissolved in pyridine (1.3 L). A first aliquot of dimethoxytrityl chloride (94.3 g, 0.278 M) is added

and the mixture stirred at room temperature for one hour. A second aliquot of dimethoxytrityl chloride (94.3 g, 0.278 M) is added and the reaction stirred for an additional one hour. Methanol (170 mL) is then added to stop the reaction. The solvent is evaporated and triturated with CH_3CN (200 mL) The residue is dissolved in CHCl (1.5 L) and extracted with 2x500 mL of saturated $NaHCO_3$ and 2x500 mL of saturated NaCl. The organic phase is dried over Na_2SO_4, filtered, and evaporated. The residue is purified on a 3.5 kg silica gel column, packed and eluted with EtOAc/hexane/ acetone (5:5:1) containing 0-5% Et_3NH. The pure fractions are evaporated to give the title product.

3'-O-Acetyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methyluridine

[00121] 2'-O-Methoxyethyl-5'-O-dimethoxytrityl-5-methyluridine (106 g, 0.167 M), DMF/pyridine (750 mL of a 3:1 mixture prepared from 562 mL of DMF and 188 mL of pyridine) and acetic anhydride (24.38 mL, 0.258 M) are combined and stirred at room temperature for 24 hours. The reaction is monitored by TLC by first quenching the TLC sample with the addition of MeOH. Upon completion of the reaction, as judged by TLC, MeOH (50 mL) is added and the mixture evaporated at 35°C. The residue is dissolved in $CHCl_3$ (800 mL) and extracted with 2x200 mL of saturated sodium bicarbonate and 2x200 mL of saturated NaCl. The water layers are back extracted with 200 mL of $CHCl_3$. The combined organics are dried with sodium sulfate and evaporated to a residue. The residue is purified on a 3.5 kg silica gel column and eluted using EtOAc/hexane(4:1). Pure product fractions are evaporated to yield the title compounds.

3'-O-Acetyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methyl-4-triazoleuridine

[00122] A first solution is prepared by dissolving 3'-O-acetyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methyluridine (96 g, 0.144 M) in CH_3CN (700 mL) and set aside. Triethylamine (189 mL, 1.44 M) is added to a solution of triazole (90 g, 1.3 M) in CH_3CN (1 L), cooled to –5°C and stirred for 0.5 h using an overhead stirrer. $POCl_3$ is added dropwise, over a 30 minute period, to the stirred solution maintained at 0-10°C, and the resulting mixture stirred for an

additional 2 hours. The first solution is added dropwise, over a 45 minute period, to the latter solution. The resulting reaction mixture is stored overnight in a cold room. Salts are filtered from the reaction mixture and the solution is evaporated. The residue is dissolved in EtOAc (1 L) and the insoluble solids are removed by filtration. The filtrate is washed with 1x300 mL of $NaHCO_3$ and 2x300 mL of saturated NaCl, dried over sodium sulfate and evaporated. The residue is triturated with EtOAc to give the title compound.

2'-O-Methoxyethyl-5'-O-dimethoxytrityl-5-methylcytidine

[00123] A solution of 3'-O-acetyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methyl-4-triazoleuridine (103 g, 0.141 M) in dioxane (500 mL) and NH_4OH (30 mL) is stirred at room temperature for 2 hours. The dioxane solution is evaporated and the residue azeotroped with MeOH (2x200 mL). The residue is dissolved in MeOH (300 mL) and transferred to a 2 liter stainless steel pressure vessel. MeOH (400 mL) saturated with NH_3 gas is added and the vessel heated to 100°C for 2 hours (TLC showed complete conversion). The vessel contents are evaporated to dryness and the residue is dissolved in EtOAc (500 mL) and washed once with saturated NaCl (200 mL). The organics are dried over sodium sulfate and the solvent is evaporated to give the title compound.

N4-Benzoyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methylcytidine

[00124] 2'-O-Methoxyethyl-5'-O-dimethoxytrityl-5-methylcytidine (85 g, 0.134 M) is dissolved in DMF (800 mL) and benzoic anhydride (37.2 g, 0.165 M) is added with stirring. After stirring for 3 hours, TLC showed the reaction to be approximately 95% complete. The solvent is evaporated and the residue azeotroped with MeOH (200 mL). The residue is dissolved in $CHCl_3$ (700 mL) and extracted with saturated NaHCO, (2x300 mL) and saturated NaCl (2x300 mL) , dried over $MgSO_4$ and evaporated to give a residue. The residue is chromatographed on a 1.5 kg silica column using EtOAc/hexane (1:1) containing 0-5% Et_3NH as the eluting solvent. The pure product fractions are evaporated to give the title compound.

N4-Benzoyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methylcytidine-3'-amidite

[00125] N4-Benzoyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methylcytidine (74 g, 0.10 M) is dissolved in CH_2Cl_2 (1 L) Tetrazole diisopropylamine (7.1 g) and 2-cyanoethoxy-tetra(isopropyl)phosphite (40.5 mL, 0.123 M) are added with stirring, under a nitrogen atmosphere. The resulting mixture is stirred for 20 hours at room temperature (TLC showed the reaction to be 95% complete). The reaction mixture is extracted with saturated $NaHCO_3$ (1x300 mL) and saturated NaCl (3x300 mL). The aqueous washes are back-extracted with CH_2Cl_2 (300 mL), and the extracts are combined, dried over $MgSO_4$, and concentrated. The residue obtained is chromatographed on a 1.5 kg silica column using EtOAc/hexane (3:1) as the eluting solvent. The pure fractions were combined to give the title compound.

2'-O-(Aminooxyethyl) nucleoside amidites and 2'-O-(dimethylaminooxyethyl) nucleoside amidites

2'-(Dimethylaminooxyethoxy) nucleoside amidites

[00126] 2'-(Dimethylaminooxyethoxy) nucleoside amidites [also known in the art as 2'-O-(dimethylaminooxyethyl) nucleoside amidites] are prepared as described in the following paragraphs. Adenosine, cytidine and guanosine nucleoside amidites are prepared similarly to the thymidine (5-methyluridine) except the exocyclic amines are protected with a benzoyl moiety in the case of adenosine and cytidine and with isobutyryl in the case of guanosine.

5'-O-tert-Butyldiphenylsilyl -O^2 -2'-anhydro-5-methyluridine

[00127] O^2 -2'-anhydro-5-methyluridine (Pro. Bio. Sint., Varese, Italy, 100.0g, 0.4'6 mmol), dimethylaminopyridine (0.66g, 0.013eq, 0.0054mmol) are dissolved in dry pyridine (500 ml) at ambient temperature under an argon atmosphere and with mechanical stirring. tert-Butyldiphenylchlorosilane (125.8g, 119.0mL, 1.1eq, 0.458mmol) is added in one portion. The reaction is stirred for 16 h at ambient temperature. TLC (Rf 0.22, ethyl acetate) indicated a

complete reaction. The solution is concentrated under reduced pressure to a thick oil. This is partitioned between dichloromethane (1 L) and saturated sodium bicarbonate (2x 1L) and brine (1L). The organic layer is dried over sodium sulfate and concentrated under reduced pressure to a thick oil. The oil is dissolved in a 1:1 mixture of ethyl acetate and ethyl ether (600mL) and the solution is cooled to –10°C. The resulting crystalline product is collected by filtration, washed with ethyl ether (3x200 mL), and dried (40°C, 1mm Hg, 24 h) to a white solid

5'-O-tert-Butyldiphenylsilyl-2'-O-(2-hydroxyethyl)-5-methyluridine

[00128] In a 2 L stainless steel, unstirred pressure reactor is added borane in tetrahydrofuran (1.0 M, 2.0 eq, 622 mL). In the fume hood and with manual stirring, ethylene glycol (350 mL, excess) is added cautiously at first until the evolution of hydrogen gas subsides. 5'-O-tert-Butyldiphenylsilyl-O^2-2'anhydro-5-methyluridine (149 g, 0.3'1 mol) and sodium bicarbonate (0.074 g, 0.003 eq) are added with manual stirring. The reactor is sealed and heated in an oil bath until an internal temperature of 160°C is reached and then maintained for 16 h (pressure < 100 psig). The reaction vessel is cooled to ambient and opened. TLC (Rf 0.67 for desired product and Rf 0.82 for ara-T side product, ethyl acetate) indicated about 70% conversion to the product. In order to avoid additional side product formation, the reaction is stopped, concentrated under reduced pressure (10 to 1mm, Hg) in a warm water bath (40-100°C) with the more extreme conditions used to remove the ethylene glycol. [Alternatively, once the low boiling solvent is gone, the remaining solution can be partitioned between ethyl acetate and water. The product will be in the organic phase.] The residue is purified by column chromatography (2kg silica gel, ethyl acetate-hexanes gradient 1:1 to 4:1). The appropriate fractions are combined, stripped, and dried to product as a white crisp foam, contaminated starting material, and pure reusable starting material.

2'-O-([2-phthalimidoxy)ethyl]-5'-t-butyldiphenylsilyl-5-methyluridine

[00129] 5'-O-tert-Butyldiphenylsilyl-2'-O-(2-hydroxyethyl)-5-methyluridine (20g, 36.98mmol) is mixed with triphenylphosphine (11.63g,

44.36mmol) and N-hydroxyphthalimide (7.24g, 44.36mmol). It is then dried over P_2O_5 under high vacuum for two days at 40°C. The reaction mixture is flushed with argon and dry THF (369.8mL, Aldrich, sure seal bottle) is added to get a clear solution. Diethyl-azodicarboxylate (6.98mL, 44.36mmol) is added dropwise to the reaction mixture. The rate of addition is maintained such that resulting deep red coloration is just discharged before adding the next drop. After the addition is complete, the reaction is stirred for 4 hrs. By that time TLC showed the completion of the reaction (ethylacetate:hexane, 60:40). The solvent is evaporated in vacuum. Residue obtained is placed on a flash column and eluted with ethyl acetate:hexane (60:40), to get 2'-O-([2-phthalimidoxy)ethyl]-5'-t-butyldiphenylsilyl-5-methyluridine as white foam.

5'-O-tert-butyldiphenylsilyl-2'-O-[(2-formadoximinooxy)ethyl]-5-methyluridine

[00130] 2'-O-([2-phthalimidoxy)ethyl]-5'-t-butyldiphenylsilyl-5-methyluridine (3.1g, 4.5mmol) is dissolved in dry CH_2C1_2 (4.5mL) and methylhydrazine (300mL, 4.64mmol) is added dropwise at –10°C to 0°C. After 1 h the mixture is filtered, the filtrate is washed with ice cold CH_2Cl_2 and the combined organic phase is washed with water, brine and dried over anhydrous Na_2SO_4. The solution is concentrated to get 2'-O(aminooxyethyl) thymidine, which is then dissolved in MeOH (67.5mL). To this formaldehyde (20% aqueous solution, w/w, 1.1 eq.) is added and the resulting mixture is stirred for 1 h. Solvent is removed under vacuum; residue chromatographed to get 5'-O-tert-butyldiphenylsilyl-2'-O-[(2-formadoximinooxy) ethyl]-5-methyluridine as white foam.

5'-O-tert-Butyldiphenylsilyl-2'-O-[N,N-dimethylaminooxyethyl]-5-methyluridine

[00131] 5'-O-tert-butyldiphenylsilyl-2'-O-[(2- formadoximinooxy)ethyl]-5-methyluridine (1.77g, 3.12mmol) is dissolved in a solution of 1M pyridinium p-toluenesulfonate (PPTS) in dry MeOH (30.6mL). Sodium cyanoborohydride (0.39g, 6.13mmol) is added to this solution at 10°C under inert atmosphere. The reaction mixture is stirred for 10 minutes at 10°C. After that the reaction vessel

is removed from the ice bath and stirred at room temperature for 2 h, the reaction monitored by TLC (5% MeOH in CH_2Cl_2). Aqueous $NaHCO_3$ solution (5%, 10mL) is added and extracted with ethyl acetate (2x20mL). Ethyl acetate phase is dried over anhydrous Na_2SO_4, evaporated to dryness. Residue is dissolved in a solution of 1M PPTS in MeOH (30.6mL). Formaldehyde (20% w/w, 30mL, 3.37mmol) is added and the reaction mixture is stirred at room temperature for 10 minutes. Reaction mixture cooled to 10°C in an ice bath, sodium cyanoborohydride (0.39g, 6.13mmol) is added, and reaction mixture stirred at 10°C for 10 minutes. After 10 minutes, the reaction mixture is removed from the ice bath and stirred at room temperature for 2 hrs. To the reaction mixture 5% $NaHCO_3$ (25mL) solution is added and extracted with ethyl acetate (2x25mL). Ethyl acetate layer is dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue obtained is purified by flash column chromatography and eluted with 5% MeOH in CH_2Cl_2 to get 5'-O-tertbutyldiphenylsilyl-2'-O-[N,N-dimethylaminooxyethyl]-5- methyluridine as a white foam.

2'-O-(dimethylaminooxyethyl)-5-methyluridine

[00132] Triethylamine trihydrofluoride (3.91mL, 24.0mmol) is dissolved in dry THF and triethylamine (1.67mL, 12mmol, dry, kept over KOH). This mixture of triethylamine-2HF is then added to 5'-O-tert-butyldiphenylsilyl-2'-O-[N,N-dimethylaminooxyethyl]-5-methyluridine (1.40g, 2.4mmol) and stirred at room temperature for 24 hrs. Reaction is monitored by TLC (5% MeOH in CH_2Cl_2). Solvent is removed under vacuum and the residue placed on a flash column and eluted with 10% MeOH in CH_2Cl_2 to get 2'-O-(dimethylaminooxyethyl)-5-methyluridine.

5'-O-DMT-2'-O-(dimethylaminooxyethyl)-5-methyluridine

[00133] 2'-O-(dimethylaminooxyethyl)-5-methyluridine (750mg, 2.17mmol) is dried over P_2O_5 under high vacuum overnight at 40°C. It is then co-evaporated with anhydrous pyridine (20mL). The residue obtained is dissolved in pyridine (11mL) under argon atmosphere. 4-dimethylaminopyridine (26.5mg, 2.60mmol), 4,4'-dimethoxytrityl chloride

(880mg, 2.60mmol) is added to the mixture and the reaction mixture is stirred at room temperature until all of the starting material disappeared. Pyridine is removed under vacuum and the residue chromatographed and eluted with 10% MeOH in CH_2C1_2 (containing a few drops of pyridine) to get 5'-O-DMT-2'-0(dimethylamino-oxyethyl)-5-methyluridine.

5'-O-DMT-2'-O-(2-N,N-dimethylaminooxyethyl)-5-methyluridine-3'-[(2-cyanoethyl)-N,N- diisopropylphosphoramidite]

[00134] 5'-O-DMT-2'-O-(dimethylaminooxyethyl)-5-methyluridine (1.08g, 1.67mmol) is co-evaporated with toluene (20mL). To the residue N,N-diisopropylamine tetrazonide (0.29g, 1.67mmol) is added and dried over P20, under high vacuum overnight at 40°C. Then the reaction mixture is dissolved in anhydrous acetonitrile (8.4mL) and 2-cyanoethyl-N,N,N^1,N^1-tetraisopropylphosphoramidite (2.12mL, 6.08mmol) is added. The reaction mixture is stirred at ambient temperature for 4 hrs under inert atmosphere. The progress of the reaction is monitored by TLC (hexane:ethyl acetate 1:1). The solvent is evaporated, then the residue is dissolved in ethyl acetate (70mL) and washed with 5% aqueous $NaHCO_3$ (40mL). Ethyl acetate layer is dried over anhydrous Na_2SO_4 and concentrated. Residue obtained is chromatographed (ethyl acetate as eluent) to get 5'-O-DMT-2'-O-(2-N,N-dimethylaminooxyethyl)-5-methyluridine-3'-[(2-cyanoethyl)-N,N-diisopropylphosphoramidite] as a foam.

2'-(Aminooxyethoxy) nucleoside amidites

[00135] 2'-(Aminooxyethoxy) nucleoside amidites [also known in the art as 2'-O-(aminooxyethyl) nucleoside amidites] are prepared as described in the following paragraphs. Adenosine, cytidine and thymidine nucleoside amidites are prepared similarly.

N2-isobutyryl-6-O-diphenylcarbamoyl-2'-O-(2-ethylacetyl)-5'-O-(4,4'-dimethoxytrityl)guanosine-3'-[(2-cyanoethyl)-N,N-diisopropylphosphoramidite]

[00136] The 2'-O-aminooxyethyl guanosine analog may be obtained by selective 2'-O-alkylation of diaminopurine riboside. Multigram quantities of diaminopurine riboside may be purchased from Schering AG (Berlin) to provide 2'-O-(2-ethylacetyl) diaminopurine riboside along with a minor amount of the 3'-O-isomer. 2'-O-(2-ethylacetyl) diaminopurine riboside may be resolved and converted to 2'-O-(2ethylacetyl)guanosine by treatment with adenosine deaminase. (McGee, D. P. C., Cook, P. D., Guinosso, C. J., WO 94/02501 Al 940203.) Standard protection procedures should afford 2'-O-(2-ethylacetyl)-5'-O-(4,4'-dimethoxytrityl)guanosine and 2-N-isobutyryl-6-O-diphenylcarbamoyl-2'-O-(2-ethylacetyl)-5'-O-(4,4'-dimethoxytrityl)guanosine which may be reduced to provide 2-N-isobutyryl-6-O-diphenylcarbamoyl-2'-O-(2-ethylacetyl)-5'-O-(4,4'-dimethoxytrityl)guanosine. As before the hydroxyl group may be displaced by N-hydroxyphthalimide via a Mitsunobu reaction, and the protected nucleoside may phosphitylated as usual to yield 2-N-isobutyryl-6-O-diphenylcarbamoyl-2'-O-(2-ethylacetyl)-5'-O-(4,4'-dimethoxytrityl)guanosine-3'-[(2-cyanoethyl)-N,N-diisopropylphosphoramiditel.

2'-dimethylaminoethoxyethoxy (2'-DMAEOE) nucleoside amidites

[00137] 2'-dimethylaminoethoxyethoxy nucleoside amidites (also known in the art as 2'-O-dimethylaminoethoxyethyl, i.e., 2'O-CH_2-O-CH_2-$N(CH_2)_2$, or 2'-DMAEOE nucleoside amidites) are prepared as follows. Other nucleoside amidites are prepared similarly.

2'-O-[2(2-N,N-dimethylaminoethoxy)ethyl]-5-methyuridine

[00138] 2[2-(Dimethylamino)ethoxylethanol (Aldrich, 6.66 g, 50 mmol) is slowly added to a solution of borane in tetrahydrofuran (1 M, 10 mL, 10 mmol) with stirring in a 100 mL bomb. Hydrogen gas evolves as the solid dissolves. O^2-, 2' - anhydro-5-methyluridine (1.2 g, 5 mmol), and sodium bicarbonate (2.5 mg) are added and the bomb is sealed, placed in an oil bath, and heated to 155°C for 26 hours. The bomb is cooled to room temperature and opened. The crude solution is concentrated and the residue partitioned between water (200 mL) and hexanes (200 mL). The excess phenol is extracted into the

hexane layer. The aqueous layer is extracted with ethyl acetate (3x200 mL) and the combined organic layers are washed once with water, dried over anhydrous sodium sulfate, and concentrated. The residue is columned on silica gel using methanol/methylene chloride 1:20 (which has 2% triethylamine) as the eluent. As the column fractions are concentrated a colorless solid forms which is collected to give the title compound as a white solid.

5'-O-dimethoxytrityl-2'-O-[2(2-N,N-dimethylaminoethoxy) ethyl)]-5-methyl uridine

[00139] To 0.5 g (1.3 mmol) of 2'-O-[2(2-N,N-imethylaminoethoxy)ethyl)1-5-methyl uridine in anhydrous pyridine (8 mL), triethylamine (0.36 mL) and dimethoxytrityl chloride (DMT-Cl, 0.87 g, 2 eq.) are added and stirred for 1 hour. The reaction mixture is poured into water (200 mL) and extracted with CH_2Cl_2 (2x200 mL) . The combined CH_2Cl_2 layers are washed with saturated $NaHCO_3$ solution, followed by saturated NaCl solution, and dried over anhydrous sodium sulfate. Evaporation of the solvent followed by silica gel chromatography using MeOH: CH_2Cl_2:Et_3N (20:1, v/v, with 1% triethylamine) gives the title compound.

5'-O-Dimethoxytrityl-2'-O-[2(2-N,N-dimethylaminoethoxy)ethyl)]-5-methyl uridine-3'-O-(cyanoethyl-N,N-diisopropyl)phosphoramidite

[00140] Diisopropylaminotetrazolide (0.6 g) and 2-cyanoethoxyN,N-diisopropyl phosphoramidite (1.1 mL, 2 eq.) are added to a solution of 5'-O-dimethoxytrityl-2'-O-[2(2-N,N-dimethylaminoethoxy)ethyl)]-5-methyluridine (2.17 g, 3 mmol) dissolved in CH_2Cl_2 (20 mL) under an atmosphere of argon. The reaction mixture is stirred overnight and the solvent evaporated. The resulting residue is purified by silica gel flash column chromatography with ethyl acetate as the eluent to give the title compound.

Example 2

Oligonucleotide synthesis

[00141] Unsubstituted and substituted phosphodiester (P=O) oligonucleotides are synthesized on an automated DNA synthesizer (Applied Biosystems model 380B) using standard phosphoramidite chemistry with oxidation by iodine.

[00142] Phosphorothioates (P=S) are synthesized as for the phosphodiester oligonucleotides except the standard oxidation bottle is replaced by 0.2 M solution of 3H-1,2-benzodithiole-3-one 1,1-dioxide in acetonitrile for the stepwise thiation of the phosphite linkages. The thiation wait step is increased to 68 sec and is followed by the capping step. After cleavage from the CPG column and deblocking in concentrated ammonium hydroxide at 55°C (18 h), the oligonucleotides are purified by precipitating twice with 2.5 volumes of ethanol from a 0.5 M NaCl solution. Phosphinate oligonucleotides are prepared as described in U.S. Patent 5,508,270, herein incorporated by reference.

[00143] Alkyl phosphonate oligonucleotides are prepared as described in U.S. Patent 4,469,863, herein incorporated by reference.

[00144] 3'-Deoxy-3'-methylene phosphonate oligonucleotides are prepared as described in U.S. Patents 5,610,289 or 5,625,050, herein incorporated by reference.

[00145] Phosphoramidite oligonucleotides are prepared as described in U.S. Patent, 5,256,775 or U.S. Patent 5,366,878, herein incorporated by reference.

[00146] Alkylphosphonothioate oligonucleotides are prepared as described in WO 94/17093 and WO 94/02499 herein incorporated by reference.

[00147] 3'-Deoxy-3'-amino phosphoramidate oligonucleotides are prepared as described in U.S. Patent 5,476,925, herein incorporated by reference.

[00148] Phosphotriester oligonucleotides are prepared as described in U.S. Patent 5,023,243, herein incorporated by reference.

[00149] Borano phosphate oligonucleotides are prepared as described in U.S. Patents 5,130,302 and 5,177,198, both herein incorporated by reference.

Example 3

Oligonucleoside Synthesis

[00150] Methylenemethylimino linked oligonucleosides, also identified as MMI linked oligonucleosides, methylenedimethylhydrazo linked oligonucleosides, also identified as MDH linked oligonucleosides, and methylenecarbonylamino linked oligonucleosides, also identified as amide-3 linked oligonucleosides, and methyleneaminocarbonyl linked oligonucleosides, also identified as amide-4 linked oligonucleosides, as well as mixed backbone compounds having, for instance, alternating MMI and P=O or P=S linkages are prepared as described in U.S. Patents 5,378,825; 5,386,023; 5,489,677; 5,602,240; and 5,610,289, all of which are herein incorporated by reference.

[00151] Formacetal and thioformacetal linked oligonucleosides are prepared as described in U.S. Patents 5,264,562 and 5,264,564, herein incorporated by reference.

[00152] Ethylene oxide linked oligonucleosides are prepared as described in U.S. Patent 5,223,618, herein incorporated by reference.

Example 4

PNA Synthesis

[00153] Peptide nucleic acids (PNAs) are prepared in accordance with any of the various procedures referred to in Peptide Nucleic Acids (PNA): Synthesis, Properties and Potential Applications, *Bioorganic & Medicinal Chemistry*, 1996, 4, 523. They may also be prepared in accordance with U.S. Patents 5,539,082; 5,700,922; and 5,719,262, herein incorporated by reference.

Example 5

Synthesis of Chimeric Oligonucleotides

[00154] Chimeric oligonucleotides, oligonucleosides, or mixed oligonucleotides/oligonucleosides of the invention can be of several different types. These include a first type wherein the "gap" segment of linked nucleosides is positioned between 5' and 3' "wing" segments of linked nucleosides and a second "open end" type wherein the "gap" segment is located

at either the 3' or the 5' terminus of the oligomeric compound. Oligonucleotides of the first type are also known in the art as "gapmers" or gapped oligonucleotides. Oligonucleotides of the second type are also known in the art as "hemimers" or "wingmers".

[2'-O-Me]--[2'-deoxy]--[2'-O-Me] Chimeric Phosphorothioate Oligonucleotides

[00155] Chimeric oligonucleotides having 2'-O-alkyl phosphorothioate and 2'-deoxy phosphorothioate oligonucleotide segments are synthesized using an Applied Biosystems automated DNA synthesizer Model 380B, as above. Oligonucleotides are synthesized using the automated synthesizer and 2'-deoxy-5'-dimethoxytrityl-3'-O-phosphoramidite for the DNA portion and 5'-dimethoxytrityl-2'-O-methyl-3'-O-phosphoramidite for 5' and 3' wings. The standard synthesis cycle is modified by increasing the wait step after the delivery of tetrazole and base to 600 s repeated four times for RNA and twice for 2'-O-methyl. The fully protected oligonucleotide is cleaved from the support and the phosphate group is deprotected in 3:1 ammonia/ethanol at room temperature overnight then lyophilized to dryness. Treatment in methanolic ammonia for 24 hrs at room temperature is then done to deprotect all bases and sample is again lyophilized to dryness. The pellet is resuspended in 1M TBAF in THF for 24 hrs at room temperature to deprotect the 2' positions. The reaction is then quenched with 1M TEAA and the sample is then reduced to 1/2 volume by rotovac before being desalted on a G25 size exclusion column. The oligo recovered is then analyzed spectrophotometrically for yield and for purity by capillary electrophoresis and by mass spectrometry.

[2'-O-(2-Methoxyethyl)]--[2'-deoxy]--[2'-O-(Methoxyethyl)] Chimeric Phosphorothioate Oligonucleotides

[00156] [2'-O-(2-methoxyethyl)]--[2'-deoxy]—[-2'-O-(methoxyethyl)] chimeric phosphorothioate oligonucleotides are prepared as per the procedure above for the 2'-O-methyl chimeric oligonucleotide, with the substitution of phorothioate oligonucleotides are prepared as per the procedure above for 2'-O-(methoxyethyl) amidites for the 2'-O-methyl amidites.

[2'-O-(2-Methoxyethyl)Phosphodiester]--[2'-deoxy Phosphorothioate]--[2'-O-(2-Methoxyethyl)] Phosphodiester] Chimeric Oligonucleotides

[00157] [2'-O-(2-methoxyethyl phosphodiester]--[2'-deoxy phosphorothioate]--[2'-O-(methcixyethyl) phosphodiester] chimeric oligonucleotides are prepared as per the above procedure for the 2'-O-methyl chimeric oligonucleotide with the substitution of 2'-O-(methoxyethyl) amidites for the 2'-O-methyl amidites, oxidization with iodine to generate the phosphodiester internucleotide linkages within the wing portions of the chimeric structures and sulfurization utilizing 3,H-1,2 benzodithiole-3-one 1,1 dioxide (Beaucage Reagent) to generate the phosphorothioate internucleotide linkages for the center gap.

[00158] Other chimeric oligonucleotides, chimeric oligonucleosides, and mixed chimeric oligonucleotides/oligonucleosides are synthesized according to United States patent 5,623,065, herein incorporated by reference.

Example 6

Oligonucleotide Isolation

[00159] After cleavage from the controlled pore glass column (Applied Biosystems) and deblocking in concentrated ammonium hydroxide at 55°C for 18 hours, the oligonucleotides or oligonucleosides are purified by precipitation twice out of 0.5 M NaCl with 2.5 volumes ethanol. Synthesized oligonucleotides are analyzed by polyacrylamide gel electrophoresis on denaturing gels and judged to be at least 85% full length material. The relative amounts of phosphorothioate and phosphodiester linkages obtained in synthesis are periodically checked by "P nuclear magnetic resonance spectroscopy, and for some studies oligonucleotides are purified by HPLC, as described by Chiang et al., *J. Biol. Chem.* 1991, 266, 18162-18171.

Example 7

Oligonucleotide Synthesis - 96 Well Plate Format

[00160] Oligonucleotides are synthesized via solid phase P(III) phosphoramidite chemistry on an automated synthesizer capable of assembling 96 sequences simultaneously in a standard 96 well format. Phosphodiester internucleotide linkages are afforded by oxidation with aqueous iodine. Phosphorothioate internucleotide linkages are generated by sulfurization utilizing 3,H-1,2 benzodithiole-3-one 1,1 dioxide (Beaucage Reagent) in anhydrous acetonitrile. Standard base-protected beta-cyanoethyldiisopropyl phosphoramidites can be purchased from commercial vendors (e.g. PE-Applied Biosystems, Foster City, CA, or Pharmacia, Piscataway, NJ). Non-standard nucleosides are synthesized as per known literature or patented methods. They are utilized as base protected betacyanoethyldiisopropyl phosphoramidites.

[00161] Oligonucleotides are cleaved from support and deprotected with concentrated NH_4OH at elevated temperature (55-60°C) for 12-16 hours and the released product then dried in vacuo. The dried product is then re-suspended in sterile water to afford a master plate from which all analytical and test plate samples are then diluted utilizing robotic pipettors.

Example 8

Oligonucleotide Analysis - 96 Well Plate Format

[00162] The concentration of oligonucleotide in each well is assessed by dilution of samples and UV absorption spectroscopy. The full-length integrity of the individual products is evaluated by capillary electrophoresis (CE) in either the 96 well format (Beckman P/ACE™ MDQ) or, for individually prepared samples, on a commercial CE apparatus (e.g., Beckman P/ACE™ 5000, ABI 270). Base and backbone composition is confirmed by mass analysis of the compounds utilizing electrospray-mass spectroscopy. All assay test plates are diluted from the master plate using single and multi-channel robotic pipettors. Plates are judged to be acceptable if at least 85% of the compounds on the plate are at least 85% full length.

Example 9

Cell culture and oligonucleotide treatment

[00163] The effect of antisense compounds on target nucleic acid expression can be tested in any of a variety of cell types provided that the target nucleic acid is present at measurable levels. This can be routinely determined using, for example, PCR or Northern blot analysis. The following 6 cell types are provided for illustrative purposes, but other cell types can be routinely used, provided that the target is expressed in the cell type chosen. This can be readily determined by methods routine in the art, for example Northern blot analysis, Ribonuclease protection assays, or RT-PCR.

T-24 cells:

[00164] The human transitional cell bladder carcinoma cell line T-24 is obtained from the American Type Culture Collection (ATCC) (Manassas, VA). T-24 cells are routinely cultured in complete McCoy's 5A basal media (Gibco/Life Technologies, Gaithersburg, MD) supplemented with 10% fetal calf serum (Gibco/Life Technologies, Gaithersburg, MD), penicillin 100 units per mL, and streptomycin 100 micrograms per mL (Gibco/Life Technologies, Gaithersburg, MD). Cells are routinely passaged by trypsinization and dilution when they reached 90% confluence. Cells are seeded into 96-well plates (Falcon-Primaria #3872) at a density of 7000 cells/well for use in RT-PCR analysis.

[00165] For Northern blotting or other analysis, cells may be seeded onto 100 mm or other standard tissue culture plates and treated similarly, using appropriate volumes of medium and oligonucleotide.

A549 cells:

[00166] The human lung carcinoma cell line A549 can be obtained from the American Type Culture Collection (ATCC) (Manassas, VA). A549 cells are routinely cultured in DMEM basal media (Gibco/Life Technologies, Gaithersburg, MD) supplemented with 10% fetal calf serum (Gibco/Life Technologies, Gaithersburg, MD), penicillin 100 units per mL, and streptomycin 100 micrograms per mL (Gibco/Life Technologies, Gaithersburg,

MD). Cells are routinely passaged by trypsinization and dilution when they reached 90% confluence.

NHDF cells:

[00167] Human neonatal dermal fibroblast (NHDF) can be obtained from the Clonetics Corporation (Walkersville MD). NHDFs are routinely maintained in Fibroblast Growth Medium (Clonetics Corporation, Walkersville MD) supplemented as recommended by the supplier. Cells are maintained for up to 10 passages as recommended by the supplier.

HEK cells:

[00168] Human embryonic keratinocytes (HEK) can be obtained from the Clonetics Corporation (Walkersville MD). HEKs are routinely maintained in Keratinocyte Growth Medium (Clonetics Corporation, Walkersville MD) formulated as recommended by the supplier. Cells are routinely maintained for up to 10 passages as recommended by the supplier.

MCF-7 cells:

[00169] The human breast carcinoma cell line MCF-7 is obtained from the American Type Culture Collection (Manassas, VA). MCF-7 cells are routinely cultured in DMEM low glucose (Gibco/Life Technologies, Gaithersburg, MD) supplemented with 10% fetal calf serum (Gibco/Life Technologies, Gaithersburg, MD). Cells are routinely passaged by trypsinization and dilution when they reached 90% confluence. Cells are seeded into 96-well plates (Falcon-Primaria #3872) at a density of 7000 cells/well for use in RT-PCR analysis.

[00170] For Northern blotting or other analyses, cells may be seeded onto 100 mm or other standard tissue culture plates and treated similarly, using appropriate volumes of medium and oligonucleotide.

LA4 cells:

[00171] The mouse lung epithelial cell line LA4 is obtained from the American Type Culture Collection (Manassas, VA). LA4 cells are routinely

cultured in F12K medium (Gibco/Life Technologies, Gaithersburg, MD) supplemented with 15% fetal calf serum (Gibco/Life Technologies, Gaithersburg, MD). Cells are routinely passaged by trypsinization and dilution when they reached 90% confluence. Cells are seeded into 96-well plates (Falcon-Primaria #3872) at a density of 3000-6000 cells/ well for use in RT-PCR analysis.

[00172] For Northern blotting or other analyses, cells may be seeded onto 100 mm or other standard tissue culture plates and treated similarly, using appropriate volumes of medium and oligonucleotide.

Treatment with antisense compounds:

[00173] When cells reached 80% confluence, they are treated with oligonucleotide. For cells grown in 96-well plates, wells are washed once with 200 µL OPTI-MEM™-1 reduced-serum medium (Gibco BRL) and then treated with 130 µL of OPTI-MEM™-1 containing 3.75 µg/mL LIPOFECTIN™ (Gibco BRL) and the desired concentration of oligonucleotide. After 4-7 hours of treatment, the medium is replaced with fresh medium. Cells are harvested 16-24 hours after oligonucleotide treatment.

[00174] The concentration of oligonucleotide used varies from cell line to cell line. To determine the optimal oligonucleotide concentration for a particular cell line, the cells are treated with a positive control oligonucleotide at a range of concentrations.

Example 10

Analysis of oligonucleotide inhibition of mPGES-1 expression

[00175] Antisense modulation of mPGES-1 expression can be assayed in a variety of ways known in the art. For example, mPGES-1 mRNA levels can be quantitated by, e.g., Northern blot analysis, competitive polymerase chain reaction (PCR), or real-time PCR (RT-PCR). Real-time quantitative PCR is presently preferred. RNA analysis can be performed on total cellular RNA or poly(A)+ mRNA. Methods of RNA isolation are taught in, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 1, pp.

4.1.1-4.2.9 and 4.5.1-4.5.3, John Wiley & Sons, Inc., 1993. Northern blot analysis is routine in the art and is taught in, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 1, pp. 4.2.1-4.2.9, John Wiley & Sons, Inc., 1996. Real-time quantitative (PCR) can be conveniently accomplished using the commercially available ABI PRISM™ 7700 Sequence Detection System, available from PE-Applied Biosystems, Foster City, CA and used according to manufacturer's instructions. Prior to quantitative PCR analysis, primer-probe sets specific to the target gene being measured are evaluated for their ability to be "multiplexed" with a GAPDH amplification reaction. In multiplexing, both the target gene and the internal standard gene GAPDH are amplified concurrently in a single sample. In this analysis, mRNA isolated from untreated cells is serially diluted. Each dilution is amplified in the presence of primer-probe sets specific for GAPDH only, target gene only ("single-plexing"), or both (multiplexing). Following PCR amplification, standard curves of GAPDH and target mRNA signal as a function of dilution are generated from both the single-plexed and multiplexed samples. If both the slope and correlation coefficient of the GAPDH and target signals generated from the multiplexed samples fall within 10% of their corresponding values generated from the single-plexed samples, the primer-probe set specific for that target is deemed as multiplexable. Other methods of PCR are also known in the art.

[00176] Protein levels of mPGES-1 can be quantitated in a variety of ways well known in the art, such as immunoprecipitation, Western blot analysis (immunoblotting), ELISA or fluorescence-activated cell sorting (FACS). Antibodies directed to mPGES-1 can be identified and obtained from a variety of sources, such as the MSRS catalog of antibodies (Aerie Corporation, Birmingham, MI), or can be prepared via conventional antibody generation methods. Methods for preparation of polyclonal antisera are taught in, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 2, pp. 11.12.1-11.12.9, John Wiley & Sons, Inc., 1997. Preparation of monoclonal antibodies is taught in, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 2, pp. 11.4.1-11.11.5, John Wiley Sons, Inc., 1997.

[00177] Immunoprecipitation methods are standard in the art and can be found at, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 2, pp. 10.16.110.16.11, John Wiley & Sons, Inc., 1998. Western blot (immunoblot) analysis is standard in the art and can be found at, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 2, pp. 10.8.1-10.8.21, John Wiley Sons, Inc., 1997. Enzyme-linked immunosorbent assays (ELISA) are standard in the art and can be found at, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 2, pp. 11.2.1-11.2.22, John Wiley & Sons, Inc., 1991.

Example 11

Poly(A)+ mRNA isolation

[00178] Poly(A)+ mRNA is isolated according to Miura et al., *Clin. Chem.*, 1996, 42, 1758-1764. Other methods for poly(A)+ mRNA isolation are taught in, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 1, pp. 4.5.1-4.5.3, John Wiley & Sons, Inc., 1993. Briefly, for cells grown on 96-well plates, growth medium is removed from the cells and each well is washed with 200 µL cold PBS. 60µL lysis buffer (10 mM Tris-HCl, pH 7.6, 1 mM EDTA, 0.5 M NaCl, 0.5% NP-40, 20 mM vanadyl-ribonucleoside complex) is added to each well, the plate is gently agitated and then incubated at room temperature for five minutes. 55 µL of lysate is transferred to Oligo d(T) coated 96-well plates (AGCT Inc., Irvine CA). Plates are incubated for 60 minutes at room temperature, washed 3 times with 200 µL of wash buffer (10 mM Tris-HCl pH 7.6, 1 mM EDTA, 0.3 M NaCl). After the final wash, the plate is blotted on paper towels to remove excess wash buffer and then air-dried for 5 minutes. 60 pL of elution buffer (5 mM Tris-HCl pH 7.6), preheated to 70°C is added to each well, the plate is incubated on a 90°C hot plate for 5 minutes, and the eluate is then transferred to a fresh 96-well plate.

[00179] Cells grown on 100 mm or other standard plates may be treated similarly, using appropriate volumes of all solutions.

Example 12

Total RNA Isolation

[00180] Total mRNA is isolated using an RNEASY 96™ kit and buffers purchased from Qiagen Inc. (Valencia CA) following the manufacturer's recommended procedures. Briefly, for cells grown on 96-well plates, growth medium is removed from the cells and each well is washed with 200 µL cold PBS. 100 µL Buffer RLT is added to each well and the plate vigorously agitated for 20 seconds. 100 µL of 70% ethanol is then added to each well and the contents mixed by pipetting three times up and down. The samples are then transferred to the RNEASY 96™ well plate attached to a QIAVAC™ manifold fitted with a waste collection tray and attached to a vacuum source. Vacuum is applied for 15 seconds. 1 mL of Buffer RW1 is added to each well of the RNEASY 96™ plate and the vacuum again applied for 15 seconds. 1 mL of Buffer RPE is then added to each well of the RNEASY 96™ plate and the vacuum applied for a period of 15 seconds. The Buffer RPE wash is then repeated and the vacuum is applied for an additional 10 minutes. The plate is then removed from the QIAVAC™ manifold and blotted dry on paper towels. The plate is then re-attached to the QIAVAC™ manifold fitted with a collection tube rack containing 1.2 mL collection tubes. RNA is then eluted by pipetting 60µL water into each well, incubating one minute, and then applying the vacuum for 30 seconds. The elution step is repeated with additional 60µL water.

[00181] The repetitive pipetting and elution steps may be automated using a QIAGEN Bio-Robot 9604 (Qiagen, Inc., Valencia CA). Essentially, after lysing of the cells on the culture plate, the plate is transferred to the robot deck where the pipetting, DNase treatment and elution steps are carried out.

Example 13

Real-time Quantitative PCR Analysis of mPGES-1 mRNA Levels

[00182] Quantitation of mPGES-1 mRNA levels is determined by real-time quantitative PCR using the ABI PRISM™ 7700 Sequence Detection System (PE-Applied Biosystems, Foster City, CA) according to manufacturer's

instructions. This is a closed-tube, non-gel-based, fluorescence detection system which allows high-throughput quantitation of polymerase chain reaction (PCR) products in real-time. As opposed to standard PCR, in which amplification products are quantitated after the PCR is completed, products in real-time quantitative PCR are quantitated as they accumulate. This is accomplished by including in the PCR reaction an oligonucleotide probe that anneals specifically between the forward and reverse PCR primers, and contains two fluorescent dyes. A reporter dye (e.g., JOE, FAM™, or VIC, obtained from either Operon Technologies Inc., Alameda, CA or PE-Applied Biosystems, Foster City, CA) is attached to the 5' end of the probe and a quencher dye (e.g., TAMRA, obtained from either Operon Technologies Inc., Alameda, CA or PE-Applied Biosystems, Foster City, CA) is attached to the 3' end of the probe. When the probe and dyes are intact, reporter dye emission is quenched by the proximity of the 3' quencher dye. During amplification, annealing of the probe to the target sequence creates a substrate that can be cleaved by the 5'-exonuclease activity of Taq polymerase. During the extension phase of the PCR amplification cycle, cleavage of the probe by Taq polymerase releases the reporter dye from the remainder of the probe (and hence from the quencher moiety) and a sequence-specific fluorescent signal is generated. With each cycle, additional reporter dye molecules are cleaved from their respective probes, and the fluorescence intensity is monitored at regular intervals by laser optics built into the ABI PRISM™ 7700 Sequence Detection System. In each assay, a series of parallel reactions containing serial dilutions of mRNA from untreated control samples generates a standard curve that is used to quantitate the percent inhibition after antisense oligonucleotide treatment of test samples.

[00183] PCR reagents can be obtained from PE-Applied Biosystems, Foster City, CA. RT-PCR reactions are carried out by adding 25μL PCR cocktail (1x TAQMAN™ buffer A, 5.5 MM $MgCl_2$, 300 μM each of dATP, dCTP and dGTP, 600 μM of dUTP, 100 nM each of forward primer, reverse primer, and probe, 20 Units RNAse inhibitor, 1.25 Units AMPLITAQ GOLD™, and 12.5 Units MuLV reverse transcriptase) to 96 well plates containing 25 μL poly(A) mRNA solution. The RT reaction is carried out by incubation for 30 minutes at 48°C. Following a 10 minute incubation at 95°C to activate the

AMPLITAQ GOLD™, 40 cycles of a two-step PCR protocol are carried out: 95°C for 15 seconds (denaturation) followed by 60°C for 1.5 minutes (annealing/extension).

[00184] Probes and primers to human mPGES-1 were designed to hybridize to a human mPGES-1 sequence, using published sequence, information (GenBank accession number NM_004878, incorporated herein as Figure 1). For human mPGES-1 the PCR primers were: forward primer: GAGACCATCTACCCCTTCCTTTTC SEQ ID NO:1802 reverse primer: TCCAGGCGACAAAAGGGTTA SEQ ID NO:1803 and the PCR probe is: FAM™-TGGGCTTCGTCTACTCCTTTCTGGGTC SEQ ID NO:1804-TAMRA where FAM™ (PE-Applied Biosystems, Foster City, CA) is the fluorescent reporter dye) and TAMRA (PE-Applied Biosystems, Foster City, CA) is the quencher dye. For human cyclophilin the PCR primers were: forward primer: CCCACCGTGTTCTTCGACAT SEQ ID NO:1805 reverse primer: TTTCTGCTGTCTTTGGGACCTT SEQ ID NO:1806 and the PCR probe is: 5' JOE- CGCGTCTCCTTTGAGCTGTTTGCA SEQ ID NO:1807 - TAMRA 3' where JOE (PE-Applied Biosystems, Foster City, CA) is the fluorescent reporter dye) and TAMRA (PE-Applied Biosystems, Foster City, CA) is the quencher dye.

Example 14

Antisense inhibition of human mPGES-1 expression by chimeric phosphorothioate oligonucleotides having 2'-MOE wings and a deoxy gap

[00185] In accordance with the present invention, a series of oligonucleotides are designed to target different regions of the human mPGES-1 RNA, using published sequences (GenBank accession number NM 004878, incorporated herein as Figure 1). The oligonucleotides are shown in Table 1. "Position" indicates the first (5'-most) nucleotide number on the particular target sequence to which the oligonucleotide binds. The indicated parameters for each oligo was predicted using RNAstructure 3.7 by David H. Mathews, Michael Zuker and Douglas H. Turner. The more negative the number, the more

likely the reaction will occur. All free energy units are in kcal/mol.) or melting temperature (The temperature at which two anneal strands of polynucleic acid separate. The higher the temperature, greater the affinity between the two strands.). When designing an antisense oligonucleotide that will bind with high affinity, it is desirable to consider the structure of the target RNA strand and the antisense oligomer. Specifically, for an oligomer to bind tightly (in the table as described as 'duplex formation'), it should be complementary to a stretch of target RNA that has little self-structure (in the table the free energy of which is described as 'target structure'). Also, the oligomer should have little self-structure, either intramolecular (in the table the free energy of which is described as 'intramolecular oligo') or bimolecular (in the table the free energy of which is described as 'intermolecular oligo'). Breaking up any self-structure amounts to a binding penalty. All compounds in Table 1 are chimeric oligonucleotides ("gapmers") 20 nucleotides in length, composed of a central "gap" region consisting of ten 2'deoxynucleotides, which is flanked on both sides (5' and 3' directions) by four-nucleotide "wings". The wings are composed of 2'-methoxyethyl (2'-MOE) nucleotides. The internucleoside (backbone) linkages are phosphorothioate (P=S) throughout the oligonucleotide. Cytidine residues in the 2'-MOE wings are 5-methylcytidines. All cytidine residues are 5-methylcytidines.

Table 1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
417	TGGGCCAGGGTGTAGGTCAC SEQ.ID.IN:1	-26	-29.1	83.6	-1.8	-1.1	-9.8
415	GGCCAGGGTGTAGGTCACGG SEQ.ID.IN:2	-25.9	-29.9	83.2	-1.8	-2.2	-10.4
416	GGGCCAGGGTGTAGGTCACG SEQ.ID.IN:3	-25.9	-29.9	83.2	-1.8	-2.2	-11
414	GCCAGGGTGTAGGTCACGGA SEQ.ID.IN:4	-25.3	-29.3	81.9	-1.8	-2.2	-7
418	CTGGGCCAGGGTGTAGGTCA SEQ.ID.IN:5	-25.2	-29.8	85	-3.5	-1	-7.6
419	GCTGGGCCAGGGTGTAGGTC SEQ.ID.IN:6	-23.2	-30.9	88.8	-7	-0.5	-7.6
494	AGGAGGCATCAGCTGCTGGT SEQ.ID.IN:7	-23.2	-28.4	82	-3.6	-1.3	-11
424	GGGGAGCTGGGCCAGGGTGT SEQ.ID.IN:8	-22.3	-32.6	90.3	-9.6	-0.5	-7.6
816	TCTTTTCACTGTTAGGGAGG SEQ.ID.IN:9	-21.6	-23	70.2	-1.3	0.1	-3.7
393	CGGATGGGTGCCCGCAGCTT SEQ.ID.IN:10	-21.3	-32.1	82.6	-9.7	-1	-9
400	CACGGAGCGGATGGGTGCCC SEQ.ID.IN:11	-21.1	-31.3	80.6	-9.5	-0.2	-8.4
423	GGGAGCTGGGCCAGGGTGTA SEQ.ID.IN:12	-20.9	-31.1	87	-9.6	-0.3	-7.6
495	AAGGAGGCATCAGCTGCTGG SEQ.ID.IN:13	-20.4	-26.5	75.6	-4	-2.1	-11
394	GCGGATGGGTGCCCGCAGCT SEQ.ID.IN:14	-20.3	-33.8	86.4	-9.7	-3.8	-12.2
493	GGAGGCATCAGCTGCTGGTC SEQ.ID.IN:15	-20.2	-28.8	83.6	-6.5	-2.1	-11
420	AGCTGGGCCAGGGTGTAGGT SEQ.ID.IN:16	-20.1	-30.5	87.1	-9.7	-0.5	-7.2
1617	GGACATTTGCAGTTTCCAAA SEQ.ID.IN:17	-20.1	-22.5	65.5	-2.4	0	-5.4
786	GATGTTTTTGATGCTCTGTT SEQ.ID.IN:18	-20	-22.1	67.8	-2.1	0	-3.6
787	TGATGTTTTTGATGCTCTGT SEQ.ID.IN:19	-19.9	-22	67.2	-2.1	0	-3.6
331	GACCAGGAAGTGCATCCAGG SEQ.ID.IN:20	-19.7	-26.6	74.3	-5.4	-1.4	-9.4
401	TCACGGAGCGGATGGGTGCC SEQ.ID.IN:21	-19.7	-29.7	79	-9.5	-0.2	-5
815	CTTTTCACTGTTAGGGAGGG SEQ.ID.IN:22	-19.7	-23.8	71.2	-3.6	-0.2	-3.1
392	GGATGGGTGCCCGCAGCTTC SEQ.ID.IN:23	-19.6	-31.7	85	-10.9	-1	-9.7
422	GGAGCTGGGCCAGGGTGTAG SEQ.ID.IN:24	-19.6	-29.9	84.6	-9.6	-0.5	-7.6
1618	GGGACATTTGCAGTTTCCAA SEQ.ID.IN:25	-19.6	-24.4	70.3	-3.9	-0.8	-6.2
428	CGCAGGGGAGCTGGGCCAGG SEQ.ID.IN:26	-19.5	-32.3	85.5	-11.3	-1.4	-9.8
427	GCAGGGGAGCTGGGCCAGGG SEQ.ID.IN:27	-19.4	-32.7	88.8	-11.8	-1.4	-9.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
783	GTTTTTGATGCTCTGTTACT SEQ.ID.IN:28	-19.3	-22.3	68.6	-3	0	-3.6
274	GCCCAGGAAAAGGAAGGGGT SEQ.ID.IN:29	-19.2	-26.1	70.8	-5.6	-1.2	-5.5
402	GTCACGGAGCGGATGGGTGC SEQ.ID.IN:30	-18.9	-28.9	79.1	-9.5	-0.1	-4.6
403	GGTCACGGAGCGGATGGGTG SEQ.ID.IN:31	-18.8	-28.3	77.3	-9.5	0.1	-4.1
1015	GAGCCAGATTGTACCACTTC SEQ.ID.IN:32	-18.7	-25.2	72.8	-6.5	0	-4.2
395	AGCGGATGGGTGCCCGCAGC SEQ.ID.IN:33	-18.6	-32.9	84.9	-9.7	-4.6	-10.9
817	CTCTTTTCACTGTTAGGGAG SEQ.ID.IN:34	-18.6	-22.7	69.5	-3.6	-0.2	-3.9
856	ATCATTAGGTTTGGGAATCT SEQ.ID.IN:35	-18.6	-21.1	64.4	-2.5	0	-3
425	AGGGGAGCTGGGCCAGGGTG SEQ.ID.IN:36	-18.5	-31.4	86.8	-12.2	-0.5	-7.6
784	TGTTTTTGATGCTCTGTTAC SEQ.ID.IN:37	-18.4	-21.4	66.3	-3	0	-3.6
1059	TGAGGCGGGAGAATCGCTTG SEQ.ID.IN:38	-18.4	-25.3	69.9	-4	-2.9	-7.9
404	AGGTCACGGAGCGGATGGGT SEQ.ID.IN:39	-18.3	-28.3	77.8	-9.5	-0.1	-4.1
861	AGATGATCATTAGGTTTGGG SEQ.ID.IN:40	-18.3	-21.1	64.6	-2.1	0	-8.7
1058	GAGGCGGGAGAATCGCTTGA SEQ.ID.IN:41	-18.3	-25.9	71.3	-4.7	-2.9	-7.9
1246	AGATGGTGGCTGAGCACAGT SEQ.ID.IN:42	-18.3	-26.1	76.2	-6.3	-1.4	-5.8
1248	CCAGATGGTGGCTGAGCACA SEQ.ID.IN:43	-18.3	-27.6	77.1	-7.7	-1.6	-5.2
782	TTTTTGATGCTCTGTTACTT SEQ.ID.IN:44	-18.2	-21.2	65.5	-3	0	-3.6
785	ATGTTTTTGATGCTCTGTTA SEQ.ID.IN:45	-18.2	-21.2	65.7	-3	0	-3.6
788	GTGATGTTTTTGATGCTCTG SEQ.ID.IN:46	-18.2	-22	67.2	-3.8	0	-3.6
492	GAGGCATCAGCTGCTGGTCA SEQ.ID.IN:47	-18.1	-28.3	81.9	-8.1	-2.1	-11
741	ATCTTCACAATCTGTCTTGA SEQ.ID.IN:48	-18.1	-21.2	65.2	-3.1	0	-4.4
1326	GCCTTGCTTCCACAGAGAAC SEQ.ID.IN:49	-18.1	-26.3	73.9	-8.2	0	-2.9
275	AGCCCAGGAAAAGGAAGGGG SEQ.ID.IN:50	-18	-24.9	68	-5.6	-1.2	-5.5
1324	CTTGCTTCCACAGAGAACTG SEQ.ID.IN:51	-18	-23.4	67.9	-4	-1.3	-6.2
280	GACGAAGCCCAGGAAAAGGA SEQ.ID.IN:52	-17.9	-23.5	64	-5.6	0	-3.5
819	CTCTCTTTTCACTGTTAGGG SEQ.ID.IN:53	-17.9	-23.4	71.6	-5.5	0	-2.7
852	TTAGGTTTGGGAATCTTAAA SEQ.ID.IN:54	-17.9	-18.4	57.4	-0.2	0	-3.4
744	TCAATCTTCACAATCTGTCT SEQ.ID.IN:55	-17.8	-20.9	64.1	-3.1	0	-2.6
818	TCTCTTTTCACTGTTAGGGA SEQ.ID.IN:56	-17.8	-23.1	71	-5.3	0	-2.9

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
849	GGTTTGGGAATCTTAAATAG SEQ.ID.IN:57	-17.8	-18.3	57	-0.2	0	-4
850	AGGTTTGGGAATCTTAAATA SEQ.ID.IN:58	-17.8	-18.3	57	-0.2	0	-4
851	TAGGTTTGGGAATCTTAAAT SEQ.ID.IN:59	-17.8	-18.3	57	-0.2	0	-4
273	CCCAGGAAAAGGAAGGGGTA SEQ.ID.IN:60	-17.7	-24	66.4	-5.6	-0.5	-4.9
552	GGAACATCAAGTCCCCAGGT SEQ.ID.IN:61	-17.7	-27.1	74.7	-9.4	0	-4
814	TTTTCACTGTTAGGGAGGGA SEQ.ID.IN:62	-17.7	-23.5	70.6	-5.3	-0.2	-3.1
1243	TGGTGGCTGAGCACAGTGAT SEQ.ID.IN:63	-17.7	-26.1	75.7	-6.8	-1.6	-6.6
1244	ATGGTGGCTGAGCACAGTGA SEQ.ID.IN:64	-17.7	-26.1	75.7	-6.8	-1.6	-6.6
421	GAGCTGGGCCAGGGTGTAGG SEQ.ID.IN:65	-17.6	-29.9	84.6	-11.6	-0.5	-7.6
1619	GGGGACATTTGCAGTTTCCA SEQ.ID.IN:66	-17.6	-26.3	75.3	-7.8	-0.8	-6.3
154	GTTGGCAAAGGCCTTCTTCC SEQ.ID.IN:67	-17.5	-27.4	76.8	-6.9	-3	-10.6
330	ACCAGGAAGTGCATCCAGGC SEQ.ID.IN:68	-17.5	-27.8	77.2	-8.7	-1.6	-9.7
37	CACCAGGCTGTGGGCAGGCA SEQ.ID.IN:69	-17.4	-31.3	85.3	-12.3	-1.5	-7.3
740	TCTTCACAATCTGTCTTGAA SEQ.ID.IN:70	-17.4	-20.5	63	-3.1	0	-3.5
813	TTTCACTGTTAGGGAGGGAG SEQ.ID.IN:71	-17.4	-23.4	70.5	-5.5	-0.2	-3.1
853	ATTAGGTTTGGGAATCTTAA SEQ.ID.IN:72	-17.4	-19.1	59.3	-1.7	0	-3.2
1325	CCTTGCTTCCACAGAGAACT SEQ.ID.IN:73	-17.4	-25.4	71.6	-8	0	-3.6
64	GAAGGCCGGGAGGGCCGGGC SEQ.ID.IN:74	-17.3	-33.9	85.3	-11.5	-5.1	-12.2
281	AGACGAAGCCCAGGAAAAGG SEQ.ID.IN:75	-17.3	-22.9	63.1	-5.6	0	-3.5
781	TTTTGATGCTCTGTTACTTT SEQ.ID.IN:76	-17.3	-21.2	65.5	-3.9	0	-3.6
1241	GTGGCTGAGCACAGTGATTC SEQ.ID.IN:77	-17.3	-25.4	75.3	-6.6	-1.4	-3.3
397	GGAGCGGATGGGTGCCCGCA SEQ.ID.IN:78	-17.2	-32.9	84.1	-11.1	-4.6	-10.7
812	TTCACTGTTAGGGAGGGAGA SEQ.ID.IN:79	-17.2	-23.9	71.5	-6.2	-0.2	-3.1
848	GTTTGGGAATCTTAAATAGA SEQ.ID.IN:80	-17.2	-17.7	55.8	-0.2	0	-4
1014	AGCCAGATTGTACCACTTCA SEQ.ID.IN:81	-17.2	-25.3	72.6	-8.1	0	-4.2
1042	TTGAACCCGGGAGGCGGAGG SEQ.ID.IN:82	-17.2	-28.8	74.7	-9.2	-2.4	-9.8
1327	AGCCTTGCTTCCACAGAGAA SEQ.ID.IN:83	-17.2	-26.1	73.6	-8.2	-0.4	-4
38	TCACCAGGCTGTGGGCAGGC SEQ.ID.IN:84	-17.1	-31	86.3	-12.3	-1.5	-7.3
820	TCTCTCTTTTCACTGTTAGG SEQ.ID.IN:85	-17.1	-22.6	70.6	-5.5	0	-2.7

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1045	CGCTTGAACCCGGGAGGCGG SEQ.ID.IN:86	-17.1	-30.5	76.3	-11.1	-2	-12.2
1422	CCAAAGCCAACGGCAAGGGA SEQ.ID.IN:87	-17.1	-26.1	68.3	-7.3	-1.7	-7.3
391	GATGGGTGCCCGCAGCTTCC SEQ.ID.IN:88	-17	-32.5	85.8	-14.3	-1	-9.7
1249	TCCAGATGGTGGCTGAGCAC SEQ.ID.IN:89	-17	-27.3	77.8	-9.2	-1	-6.2
102	ACGTACATCTTGATGACCAG SEQ.ID.IN:90	-16.9	-22.3	64.9	-4.1	-1.2	-9.4
398	CGGAGCGGATGGGTGCCCGC SEQ.ID.IN:91	-16.9	-33	82.6	-12.6	-3.5	-9.7
745	ATCAATCTTCACAATCTGTC SEQ.ID.IN:92	-16.9	-20	62.1	-3.1	0	-2.6
862	CAGATGATCATTAGGTTTGG SEQ.ID.IN:93	-16.9	-20.6	63.2	-3	0	-8.7
1043	CTTGAACCCGGGAGGCGGAG SEQ.ID.IN:94	-16.9	-28.5	74.1	-9.2	-2.4	-10.7
277	GAAGCCCAGGAAAAGGAAGG SEQ.ID.IN:95	-16.8	-22.4	62.6	-5.6	0	-3.4
405	TAGGTCACGGAGCGGATGGG SEQ.ID.IN:96	-16.8	-26.8	73.9	-9.5	-0.1	-4.1
406	GTAGGTCACGGAGCGGATGG SEQ.ID.IN:97	-16.8	-26.8	74.7	-9.5	-0.1	-4.1
1239	GGCTGAGCACAGTGATTCAT SEQ.ID.IN:98	-16.8	-24.9	73	-6.6	-1.4	-7.8
1240	TGGCTGAGCACAGTGATTCA SEQ.ID.IN:99	-16.8	-24.9	72.9	-6.6	-1.4	-7.8
1616	GACATTTGCAGTTTCCAAAC SEQ.ID.IN:100	-16.8	-21.5	63.5	-3.9	-0.6	-5.3
36	ACCAGGCTGTGGGCAGGCAT SEQ.ID.IN:101	-16.7	-30.6	84.3	-12.3	-1.5	-7.3
65	GGAAGGCCGGGAGGGCCGGG SEQ.ID.IN:102	-16.7	-33.3	83.6	-11.5	-5.1	-10.8
1016	TGAGCCAGATTGTACCACTT SEQ.ID.IN:103	-16.7	-24.8	71	-8.1	0	-4.2
279	ACGAAGCCCAGGAAAAGGAA SEQ.ID.IN:104	-16.6	-22.2	61.1	-5.6	0	-3.5
286	GGAGTAGACGAAGCCCAGGA SEQ.ID.IN:105	-16.6	-26.5	72.9	-9.9	0	-3.5
332	AGACCAGGAAGTGCATCCAG SEQ.ID.IN:106	-16.6	-25.4	72	-7.2	-1.5	-8.7
735	ACAATCTGTCTTGAAATGGT SEQ.ID.IN:107	-16.6	-19.7	60.1	-3.1	0	-4.4
846	TTGGGAATCTTAAATAGAGT SEQ.ID.IN:108	-16.6	-17.6	55.7	-0.2	-0.1	-2.9
1060	CTGAGGCGGGAGAATCGCTT SEQ.ID.IN:109	-16.6	-26.2	71.8	-7.5	-2.1	-7.1
276	AAGCCCAGGAAAAGGAAGGG SEQ.ID.IN:110	-16.5	-23	63.8	-5.6	-0.8	-5.2
496	CAAGGAGGCATCAGCTGCTG SEQ.ID.IN:111	-16.5	-26	74.1	-7.4	-2.1	-10.4
1219	GCCTGTCATCCCAGCACTTT SEQ.ID.IN:112	-16.5	-29.9	82.6	-13.4	0	-4.1
272	CCAGGAAAAGGAAGGGGTAG SEQ.ID.IN:113	-16.4	-22	63.2	-5.6	0	-3.1
278	CGAAGCCCAGGAAAAGGAAG SEQ.ID.IN:114	-16.4	-22	60.8	-5.6	0	-3.4

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
730	CTGTCTTGAAATGGTTCCCA SEQ.ID.IN:115	-16.4	-24.3	69.4	-7.2	-0.5	-4
409	GGTGTAGGTCACGGAGCGGA SEQ.ID.IN:116	-16.3	-28	78.2	-9.5	-2.2	-7.5
748	TCTATCAATCTTCACAATCT SEQ.ID.IN:117	-16.3	-19.4	60.4	-3.1	0	-1.1
1046	TCGCTTGAACCCGGGAGGCG SEQ.ID.IN:118	-16.3	-29.7	75.5	-11.1	-1.3	-12.6
1450	GCCAGAGAGAAGACTGCAGC SEQ.ID.IN:119	-16.3	-25.6	73.2	-8.5	-0.3	-8.9
551	GAACATCAAGTCCCCAGGTA SEQ.ID.IN:120	-16.2	-25.6	71.7	-9.4	0	-3.3
746	TATCAATCTTCACAATCTGT SEQ.ID.IN:121	-16.2	-19.3	60	-3.1	0	-2.5
1321	GCTTCCACAGAGAACTGGCA SEQ.ID.IN:122	-16.2	-26.1	73.6	-8.2	-1.7	-6.9
1428	AGACATCCAAAGCCAACGGC SEQ.ID.IN:123	-16.2	-25	67.6	-7.3	-1.4	-6.3
373	CCCCAGGTAGGCCACGGTGT SEQ.ID.IN:124	-16.1	-33.1	86.3	-16.3	-0.5	-7.7
731	TCTGTCTTGAAATGGTTCCC SEQ.ID.IN:125	-16.1	-24	69.9	-7.2	-0.5	-3.1
736	CACAATCTGTCTTGAAATGG SEQ.ID.IN:126	-16.1	-19.2	58.4	-3.1	0	-4.4
789	AGTGATGTTTTTGATGCTCT SEQ.ID.IN:127	-16.1	-22	67.6	-5.9	0	-3.6
1253	AAACTCCAGATGGTGGCTGA SEQ.ID.IN:128	-16.1	-24.3	69.2	-7.5	-0.4	-5.1
1328	CAGCCTTGCTTCCACAGAGA SEQ.ID.IN:129	-16.1	-27.5	77.2	-10.7	-0.5	-4.2
1423	TCCAAAGCCAACGGCAAGGG SEQ.ID.IN:130	-16.1	-25.9	68.5	-7.3	-2.5	-8.5
1711	AATCACACATCTCAGGTCAC SEQ.ID.IN:131	-16.1	-22.3	67.1	-6.2	0	-2.5
63	AAGGCCGGGAGGGCCGGGCT SEQ.ID.IN:132	-16	-34.2	85.8	-13.1	-5.1	-13
287	AGGAGTAGACGAAGCCCAGG SEQ.ID.IN:133	-16	-25.9	71.9	-9.9	0	-3.5
388	GGGTGCCCGCAGCTTCCCCA SEQ.ID.IN:134	-16	-36.6	92	-18.4	-2.2	-9.1
858	TGATCATTAGGTTTGGGAAT SEQ.ID.IN:135	-16	-20.4	62.2	-4.4	0	-6
908	AATTTCTGGGGTCAGTCTGA SEQ.ID.IN:136	-16	-23.8	71.7	-7.1	-0.5	-6.8
1047	ATCGCTTGAACCCGGGAGGC SEQ.ID.IN:137	-16	-28.9	75.7	-11.1	-1.1	-11.5
1661	ACACACACACACACACACAC SEQ.ID.IN:138	-16	-22.3	64.2	-6.3	0	0
1662	CACACACACACACACACACA SEQ.ID.IN:139	-16	-22.8	64.8	-6.8	0	0
1664	CACACACACACACACACACA SEQ.ID.IN:140	-16	-22.8	64.8	-6.8	0	0
1666	CACACACACACACACACACA SEQ.ID.IN:141	-16	-22.8	64.8	-6.8	0	0
1667	ACACACACACACACACACAC SEQ.ID.IN:142	-16	-22.3	64.2	-6.3	0	0
1705	ACATCTCAGGTCACGGGTCT SEQ.ID.IN:143	-16	-26.7	77.7	-10.7	0	-3.5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	TTGGCAAAGGCCTTCTTCCG						
153	SEQ.ID.IN:144	-15.9	-27	73.3	-8.1	-3	-10.9
	GGAAGGGGTAGATGGTCTCC						
263	SEQ.ID.IN:145	-15.9	-26.3	76.5	-9.9	-0.2	-4
	GGTGCCCGCAGCTTCCCCAG						
387	SEQ.ID.IN:146	-15.9	-35.4	90	-18.4	-1	-0.5
	CAGGGTGTAGGTCACGGAGC						
412	SEQ.ID.IN:147	-15.9	-27.3	78.6	-9.2	-2.2	-5
	CTATCAATCTTCACAATCTG						
747	SEQ.ID.IN:148	-15.9	-19	58.9	-3.1	0	-1.8
	TTTGATGCTCTGTTACTTTA						
780	SEQ.ID.IN:149	-15.9	-20.8	64.5	-4.9	0	-3.6
	GACATCCAAAGCCAACGGCA						
1427	SEQ.ID.IN:150	-15.9	-25.7	68.4	-7.3	-2.5	-7.6
	AGGGGACATTTGCAGTTTCC						
1620	SEQ.ID.IN:151	-15.9	-25.6	74.5	-9.7	0	-5.2
	TAGACGAAGCCCAGGAAAAG						
282	SEQ.ID.IN:152	-15.8	-21.4	60.4	-5.6	0	-3.5
	GTGTAGGTCACGGAGCGGAT						
408	SEQ.ID.IN:153	-15.8	-26.8	75.5	-9.5	-1.4	-6.1
	CCAGGGTGTAGGTCACGGAG						
413	SEQ.ID.IN:154	-15.8	-27.5	77.7	-10.2	-1.4	-7
	CAATCTGTCTTGAAATGGTT						
734	SEQ.ID.IN:155	-15.8	-19.6	59.9	-3.8	0	-2.5
	CTTCACAATCTGTCTTGAAA						
739	SEQ.ID.IN:156	-15.8	-19.4	59.5	-3.1	-0.1	-3.6
	TGCCTGTCATCCCAGCACTT						
1220	SEQ.ID.IN:157	-15.8	-29.8	82	-13.4	-0.3	-4.1
	CAGATGGTGGCTGAGCACAG						
1247	SEQ.ID.IN:158	-15.8	-25.6	73.8	-8.2	-1.6	-2.6
	CACATCTCAGGTCACGGGTC						
1706	SEQ.ID.IN:159	-15.8	-26.5	76.8	-10.7	0	-3.5
	CATTAGGTTTGGGAATCTTA						
854	SEQ.ID.IN:160	-15.7	-20.5	62.7	-4.8	0	-2.9
	GGGCTGCTCATCACCAGGCT						
48	SEQ.ID.IN:161	-15.6	-30.8	85.6	-14.2	-0.9	-6.5
	TGTAGGTCACGGAGCGGATG						
407	SEQ.ID.IN:162	-15.6	-25.6	72	-9.5	-0.1	-4.2
	AACATCAAGTCCCCAGGTAT						
550	SEQ.ID.IN:163	-15.6	-25	70.3	-9.4	0	-3.3
	AGGAACATCAAGTCCCCAGG						
553	SEQ.ID.IN:164	-15.6	-25.9	71.8	-9.4	-0.8	-4.7
	GCTGAGCACAGTGATTCATG						
1238	SEQ.ID.IN:165	-15.6	-23.7	70.2	-6.6	-1.4	-7.8
	GGGGTTGGCAAAGGCCTTCT						
157	SEQ.ID.IN:166	-15.5	-28.5	78.9	-10	-3	-10.6
	AGGCATCAGCTGCTGGTCAC						
491	SEQ.ID.IN:167	-15.5	-27.9	81.1	-10.3	-2.1	-11
	TTCTATCAATCTTCACAATC						
749	SEQ.ID.IN:168	-15.5	-18.6	58.8	-3.1	0	-1.1
	TTTGGGAATCTTAAATAGAG						
847	SEQ.ID.IN:169	-15.5	-16.5	53.1	-0.2	-0.1	-3.2
	ATTTCTGGGGTCAGTCTGAA						
907	SEQ.ID.IN:170	-15.5	-23.8	71.7	-7.1	-1.1	-6.8
	GAATTTCTGGGGTCAGTCTG						
909	SEQ.ID.IN:171	-15.5	-23.8	71.7	-7.1	-1.1	-8.4
	AGAATTTCTGGGGTCAGTCT						
910	SEQ.ID.IN:172	-15.5	-23.8	72.2	-7.1	-1.1	-8.4

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
950	AAATACAGATGGCCAGGCTT SEQ.ID.IN:173	-15.5	-23.5	66.8	-7.1	-0.4	-9.1
1322	TGCTTCCACAGAGAACTGGC SEQ.ID.IN:174	-15.5	-25.4	72.3	-8.2	-1.7	-6.7
1663	ACACACACACACACACACAC SEQ.ID.IN:175	-15.5	-22.3	64.2	-6.8	0	0
1665	ACACACACACACACACACAC SEQ.ID.IN:176	-15.5	-22.3	64.2	-6.8	0	0
1704	CATCTCAGGTCACGGGTCTA SEQ.ID.IN:177	-15.5	-26.2	76.4	-10.7	0	-3.5
1771	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:178	-15.5	-15.9	53.7	0	0	0
1772	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:179	-15.5	-15.9	53.7	0	0	0
1773	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:180	-15.5	-15.9	53.7	0	0	0
1774	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:181	-15.5	-15.9	53.7	0	0	0
1775	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:182	-15.5	-15.9	53.7	0	0	0
1776	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:183	-15.5	-15.9	53.7	0	0	0
1777	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:184	-15.5	-15.9	53.7	0	0	0
1778	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:185	-15.5	-15.9	53.7	0	0	0
1779	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:186	-15.5	-15.9	53.7	0	0	0
1780	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:187	-15.5	-15.9	53.7	0	0	0
1781	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:188	-15.5	-15.9	53.7	0	0	0
1782	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:189	-15.5	-15.9	53.7	0	0	0
1783	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:190	-15.5	-15.9	53.7	0	0	0
1784	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:191	-15.5	-15.9	53.7	0	0	0
1785	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:192	-15.5	-15.9	53.7	0	0	0
1786	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:193	-15.5	-15.9	53.7	0	0	0
1787	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:194	-15.5	-15.9	53.7	0	0	0
1788	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:195	-15.5	-15.9	53.7	0	0	0
1789	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:196	-15.5	-15.9	53.7	0	0	0
1790	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:197	-15.5	-15.9	53.7	0	0	0
1791	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:198	-15.5	-15.9	53.7	0	0	0
1792	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:199	-15.5	-15.9	53.7	0	0	0
1793	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:200	-15.5	-15.9	53.7	0	0	0
1794	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:201	-15.5	-15.9	53.7	0	0	0

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1795	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:202	-15.5	-15.9	53.7	0	0	0
1796	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:203	-15.5	-15.9	53.7	0	0	0
1797	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:204	-15.5	-15.9	53.7	0	0	0
1798	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:205	-15.5	-15.9	53.7	0	0	0
1799	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:206	-15.5	-15.9	53.7	0	0	0
1800	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:207	-15.5	-15.9	53.7	0	0	0
1801	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:208	-15.5	-15.9	53.7	0	0	0
152	TGGCAAAGGCCTTCTTCCGC SEQ.ID.IN:209	-15.4	-28.7	77	-10.3	-3	-10.9
738	TTCACAATCTGTCTTGAAAT SEQ.ID.IN:210	-15.4	-18.5	57.6	-3.1	0	-3.5
811	TCACTGTTAGGGAGGGAGAG SEQ.ID.IN:211	-15.4	-23.8	71.4	-8.4	0	-2.8
1221	ATGCCTGTCATCCCAGCACT SEQ.ID.IN:212	-15.4	-29.7	81.6	-13.4	-0.7	-4.5
1466	TCCCACCCACACCTGAGCCA SEQ.ID.IN:213	-15.4	-33.1	83.8	-17.7	0	-3.2
39	ATCACCAGGCTGTGGGCAGG SEQ.ID.IN:214	-15.3	-29.2	81.6	-12.3	-1.5	-6.9
49	CGGGCTGCTCATCACCAGGC SEQ.ID.IN:215	-15.3	-30.7	82.9	-14.4	-0.9	-6.5
103	CACGTACATCTTGATGACCA SEQ.ID.IN:216	-15.3	-23	65.8	-5.9	-1.8	-9.6
151	GGCAAAGGCCTTCTTCCGCA SEQ.ID.IN:217	-15.3	-29.4	78.2	-11.8	-2.3	-10.6
546	TCAAGTCCCCAGGTATAGCC SEQ.ID.IN:218	-15.3	-28.3	78.6	-13	0	-3.3
737	TCACAATCTGTCTTGAAATG SEQ.ID.IN:219	-15.3	-18.4	57.2	-3.1	0	-4.4
751	TTTTCTATCAATCTTCACAA SEQ.ID.IN:220	-15.3	-18.4	58.1	-3.1	0	-1.1
752	ATTTTCTATCAATCTTCACA SEQ.ID.IN:221	-15.3	-19.1	60.1	-3.8	0	-1.5
821	TTCTCTCTTTTCACTGTTAG SEQ.ID.IN:222	-15.3	-21.5	68.1	-6.2	0	-2.7
911	CAGAATTTCTGGGGTCAGTC SEQ.ID.IN:223	-15.3	-23.6	71.3	-7.1	-1.1	-8.6
1041	TGAACCCGGGAGGCGGAGGC SEQ.ID.IN:224	-15.3	-30.5	78.2	-13.1	-1.9	-11.7
1044	GCTTGAACCCGGGAGGCGGA SEQ.ID.IN:225	-15.3	-30.3	77.7	-12.6	-2.4	-10.7
201	TCGCTCCTGCAATACTGGGG SEQ.ID.IN:226	-15.2	-27.4	75	-10.8	-1.3	-4.9
549	ACATCAAGTCCCCAGGTATA SEQ.ID.IN:227	-15.2	-25.4	72.1	-10.2	0	-3.3
750	TTTCTATCAATCTTCACAAT SEQ.ID.IN:228	-15.2	-18.3	57.7	-3.1	0	-1.1
855	TCATTAGGTTTGGGAATCTT SEQ.ID.IN:229	-15.2	-21.2	64.8	-6	0	-3
912	CCAGAATTTCTGGGGTCAGT SEQ.ID.IN:230	-15.2	-25.2	73.4	-7.1	-2.9	-12.2

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1048	AATCGCTTGAACCCGGGAGG SEQ.ID.IN:231	-15.2	-26.4	69.8	-9.5	-0.9	-11.5
1224	TTCATGCCTGTCATCCCAGC SEQ.ID.IN:232	-15.2	-29.1	81.2	-13.9	0	-5.5
1429	AAGACATCCAAAGCCAACGG SEQ.ID.IN:233	-15.2	-22.5	62	-7.3	0	-3.5
1449	CCAGAGAGAAGACTGCAGCA SEQ.ID.IN:234	-15.2	-24.5	70	-8.5	-0.3	-8.9
1712	AAATCACACATCTCAGGTCA SEQ.ID.IN:235	-15.2	-21.4	64.3	-6.2	0	-2.5
156	GGGTTGGCAAAGGCCTTCTT SEQ.ID.IN:236	-15.1	-27.4	76.7	-10	-2.3	-10.6
262	GAAGGGGTAGATGGTCTCCA SEQ.ID.IN:237	-15.1	-25.8	74.9	-9.9	-0.6	-4.5
1057	AGGCGGGAGAATCGCTTGAA SEQ.ID.IN:238	-15.1	-24.6	67.9	-6.6	-2.9	-7.9
1223	TCATGCCTGTCATCCCAGCA SEQ.ID.IN:239	-15.1	-29.7	81.8	-13.9	-0.5	-5.5
271	CAGGAAAAGGAAGGGGTAGA SEQ.ID.IN:240	-15	-20.6	60.8	-5.6	0	-0.7
329	CCAGGAAGTGCATCCAGGCG SEQ.ID.IN:241	-15	-28.4	76.4	-11.8	-1.5	-8.8
378	AGCTTCCCCAGGTAGGCCAC SEQ.ID.IN:242	-15	-31.9	86.5	-15.6	-1.2	-7.7
497	CCAAGGAGGCATCAGCTGCT SEQ.ID.IN:243	-15	-28	77.9	-10.9	-2.1	-8.3
859	ATGATCATTAGGTTTGGGAA SEQ.ID.IN:244	-15	-20.4	62.2	-4.9	0	-7.7
1245	GATGGTGGCTGAGCACAGTG SEQ.ID.IN:245	-15	-26.1	75.7	-9.5	-1.6	-6.6
1465	CCCACCCACACCTGAGCCAG SEQ.ID.IN:246	-15	-32.7	82.5	-17.7	0	-5.6
35	CCAGGCTGTGGGCAGGCATC SEQ.ID.IN:247	-14.9	-30.8	85.6	-14.3	-1.5	-6.6
267	AAAAGGAAGGGGTAGATGGT SEQ.ID.IN:248	-14.9	-20.5	61.1	-5.6	0	-1.1
283	GTAGACGAAGCCCAGGAAAA SEQ.ID.IN:249	-14.9	-22.6	62.9	-7.7	0	-3.4
326	GGAAGTGCATCCAGGCGACA SEQ.ID.IN:250	-14.9	-27.2	74.5	-11.4	-0.8	-8
426	CAGGGGAGCTGGGCCAGGGT SEQ.ID.IN:251	-14.9	-32.1	88.1	-16.3	-0.7	-9.1
556	GGAAGGAACATCAAGTCCCC SEQ.ID.IN:252	-14.9	-25.1	69.5	-9.4	-0.6	-4.8
743	CAATCTTCACAATCTGTCTT SEQ.ID.IN:253	-14.9	-20.6	63	-5.7	0	-2.6
1017	GTGAGCCAGATTGTACCACT SEQ.ID.IN:254	-14.9	-25.9	74	-11	0	-4.2
1242	GGTGGCTGAGCACAGTGATT SEQ.ID.IN:255	-14.9	-26.2	76.3	-9.7	-1.6	-6.6
1424	ATCCAAAGCCAACGGCAAGG SEQ.ID.IN:256	-14.9	-24.7	66.2	-7.3	-2.5	-8.3
200	CGCTCCTGCAATACTGGGGG SEQ.ID.IN:257	-14.8	-28.2	75.8	-12	-1.3	-4.9
375	TTCCCCAGGTAGGCCACGGT SEQ.ID.IN:258	-14.8	-32.4	85.2	-16.3	-1.2	-7.7
490	GGCATCAGCTGCTGGTCACA SEQ.ID.IN:259	-14.8	-28.6	81.8	-11.7	-2.1	-10.4

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	TTTCTGGGGTCAGTCTGAAA						
906	SEQ.ID.IN:260	-14.8	-23.1	69.2	-7.1	-1.1	-6.8
	GGAGAATCGCTTGAACCCGG						
1052	SEQ.ID.IN:261	-14.8	-25.8	68.7	-10.1	-0.8	-6.6
	TTTTTTTTTTTTTTTTTTTT						
1770	SEQ.ID.IN:262	-14.8	-15.9	53.7	-1	0	0
	AGGAAGGCCGGGAGGGCCGG						
66	SEQ.ID.IN:263	-14.7	-32.1	81.6	-13.1	-4.3	-10.2
	TCCCCAGGTAGGCCACGGTG						
374	SEQ.ID.IN:264	-14.7	-32.3	84.6	-16.3	-1.2	-7.7
	AAAATACAGATGGCCAGGCT						
951	SEQ.ID.IN:265	-14.7	-22.7	64.5	-7.1	-0.4	-9.1
	CCTGTCATCCCAGCACTTTG						
1218	SEQ.ID.IN:266	-14.7	-28.1	78	-13.4	0	-4.1
	GGGCCGGGCTGCTCATCACC						
53	SEQ.ID.IN:267	-14.6	-33.2	87.5	-17.6	-0.4	-9.8
	CATCAAGTCCCCAGGTATAG						
548	SEQ.ID.IN:268	-14.6	-25.2	71.8	-10.6	0	-3.3
	GAGAATCGCTTGAACCCGGG						
1051	SEQ.ID.IN:269	-14.6	-25.8	68.7	-10.1	0	-10.2
	ACATCCAAAGCCAACGGCAA						
1426	SEQ.ID.IN:270	-14.6	-24.4	65.3	-7.3	-2.5	-7.6
	ACGGAGCGGATGGGTGCCCG						
399	SEQ.ID.IN:271	-14.5	-31.4	79.3	-14.1	-2.8	-9.8
	GCCAGATTGTACCACTTCAC						
1013	SEQ.ID.IN:272	-14.5	-25.5	72.9	-11	0	-4.2
	CTCCAGATGGTGGCTGAGCA						
1250	SEQ.ID.IN:273	-14.5	-28	79.1	-12.4	-1	-6.2
	TTTTTTTTTTTTTTTTTTTT						
1763	SEQ.ID.IN:274	-14.5	-15.9	53.7	-1.3	0	0
	TTTTTTTTTTTTTTTTTTTT						
1764	SEQ.ID.IN:275	-14.5	-15.9	53.7	-1.3	0	0
	TTTTTTTTTTTTTTTTTTTT						
1765	SEQ.ID.IN:276	-14.5	-15.9	53.7	-1.3	0	0
	TTTTTTTTTTTTTTTTTTTT						
1766	SEQ.ID.IN:277	-14.5	-15.9	53.7	-1.3	0	0
	CAAGTCCCCAGGTATAGCCA						
545	SEQ.ID.IN:278	-14.4	-28.6	77.9	-13	-1.1	-4.6
	CATCAGCCACTTCGTGCAGG						
712	SEQ.ID.IN:279	-14.4	-27.6	76.8	-13.2	0.1	-5.5
	AATACAGATGGCCAGGCTTG						
949	SEQ.ID.IN:280	-14.4	-24.2	68.9	-8.9	-0.4	-9.1
	AAAACTCCAGATGGTGGCTG						
1254	SEQ.ID.IN:281	-14.4	-23	65.7	-7.5	-1	-5.5
	CATCCAAAGCCAACGGCAAG						
1425	SEQ.ID.IN:282	-14.4	-24.2	65	-7.3	-2.5	-7.6
	AGCCAGAGAGAAGACTGCAG						
1451	SEQ.ID.IN:283	-14.4	-23.8	69.2	-8.5	-0.8	-8.6
	GAAAAGGAAGGGGTAGATGG						
268	SEQ.ID.IN:284	-14.3	-19.9	59.4	-5.6	0	-1.1
	GGAAAAGGAAGGGGTAGATG						
269	SEQ.ID.IN:285	-14.3	-19.9	59.4	-5.6	0	-1.1
	AGGAAAAGGAAGGGGTAGAT						
270	SEQ.ID.IN:286	-14.3	-19.9	59.6	-5.6	0	-1.1
	GTGCCCGCAGCTTCCCCAGG						
386	SEQ.ID.IN:287	-14.3	-35.4	90	-20	-1	-5.9
	GAAGGAACATCAAGTCCCCA						
555	SEQ.ID.IN:288	-14.3	-24.6	68.1	-9.4	-0.8	-3.9

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1615	ACATTTGCAGTTTCCAAACC SEQ.ID.IN:289	-14.3	-22.9	65.9	-7.8	-0.6	-5.3
333	AAGACCAGGAAGTGCATCCA SEQ.ID.IN:290	-14.2	-24.7	69.5	-8.9	-1.5	-8.7
742	AATCTTCACAATCTGTCTTG SEQ.ID.IN:291	-14.2	-19.9	61.6	-5.7	0	-4.3
779	TTGATGCTCTGTTACTTTAG SEQ.ID.IN:292	-14.2	-20.7	64.4	-6.5	0	-3.3
52	GGCCGGGCTGCTCATCACCA SEQ.ID.IN:293	-14.1	-32.7	85.9	-17.6	-0.4	-9.8
284	AGTAGACGAAGCCCAGGAAA SEQ.ID.IN:294	-14.1	-23.3	65	-9.2	0	-3.5
288	AAGGAGTAGACGAAGCCCAG SEQ.ID.IN:295	-14.1	-24	67.3	-9.9	0	-3.5
411	AGGGTGTAGGTCACGGAGCG SEQ.ID.IN:296	-14.1	-27.4	77.2	-11.1	-2.2	-6.3
860	GATGATCATTAGGTTTGGGA SEQ.ID.IN:297	-14.1	-21.7	65.7	-6.9	0	-8.7
1061	GCTGAGGCGGGAGAATCGCT SEQ.ID.IN:298	-14.1	-27.9	75.5	-10.9	-2.9	-7.9
1233	GCACAGTGATTCATGCCTGT SEQ.ID.IN:299	-14.1	-26.3	75.7	-11.4	-0.6	-7
1255	TAAAACTCCAGATGGTGGCT SEQ.ID.IN:300	-14.1	-22.7	65.3	-7.5	-1	-5.5
1329	CCAGCCTTGCTTCCACAGAG SEQ.ID.IN:301	-14.1	-28.9	79.3	-14.1	-0.5	-4.2
58	CGGGAGGGCCGGGCTGCTCA SEQ.ID.IN:302	-14	-33.7	86.8	-17.6	-1.9	-11.9
202	GTCGCTCCTGCAATACTGGG SEQ.ID.IN:303	-14	-27.4	75.8	-12	-1.3	-5.1
265	AAGGAAGGGGTAGATGGTCT SEQ.ID.IN:304	-14	-23.2	68.8	-9.2	0	-2.7
822	CTTCTCTCTTTTCACTGTTA SEQ.ID.IN:305	-14	-22.4	69.9	-8.4	0	-2.7
905	TTCTGGGGTCAGTCTGAAAA SEQ.ID.IN:306	-14	-22.3	66.5	-7.1	-1.1	-6.8
1049	GAATCGCTTGAACCCGGGAG SEQ.ID.IN:307	-14	-25.8	68.7	-10.1	0	-11.5
1050	AGAATCGCTTGAACCCGGGA SEQ.ID.IN:308	-14	-25.8	68.7	-10.1	0	-11.5
1323	TTGCTTCCACAGAGAACTGG SEQ.ID.IN:309	-14	-23.7	68.5	-8	-1.7	-6.7
1570	GTTCCTTTGAGTGGCTGGTC SEQ.ID.IN:310	-14	-27.3	81.3	-13.3	0	-4.4
1769	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:311	-14	-15.9	53.7	-1.9	0	0
257	GGTAGATGGTCTCCATGTCG SEQ.ID.IN:312	-13.9	-25.9	75.3	-10.9	-1	-5.9
266	AAAGGAAGGGGTAGATGGTC SEQ.ID.IN:313	-13.9	-21.6	64.6	-7.7	0	-1.8
429	GCGCAGGGGAGCTGGGCCAG SEQ.ID.IN:314	-13.9	-32.9	87.3	-14.8	-4.2	-9.8
857	GATCATTAGGTTTGGGAATC SEQ.ID.IN:315	-13.9	-20.8	63.8	-6.9	0	-4.7
1657	ACACACACACACACACACAC SEQ.ID.IN:316	-13.9	-22.3	64.2	-8.4	0	0
1658	CACACACACACACACACACA SEQ.ID.IN:317	-13.9	-22.8	64.8	-8.9	0	0

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1660	CACACACACACACACACACA SEQ.ID.IN:318	-13.9	-22.8	64.8	-8.9	0	0
1668	CACACACACACACACACACA SEQ.ID.IN:319	-13.9	-22.8	64.8	-8.9	0	0
1670	CACACACACACACACACACA SEQ.ID.IN:320	-13.9	-22.8	64.8	-8.9	0	0
1671	ACACACACACACACACACAC SEQ.ID.IN:321	-13.9	-22.3	64.2	-8.4	0	0
62	AGGCCGGGAGGGCCGGGCTG SEQ.ID.IN:322	-13.8	-34.9	88.1	-16	-5.1	-13
390	ATGGGTGCCCGCAGCTTCCC SEQ.ID.IN:323	-13.8	-33.9	87.8	-17.6	-2.5	-9.7
913	GCCAGAATTTCTGGGGTCAG SEQ.ID.IN:324	-13.8	-25.8	74.3	-8.4	-3.6	-13.5
1454	CTGAGCCAGAGAGAAGACTG SEQ.ID.IN:325	-13.8	-22.8	66.7	-8.5	-0.1	-5.4
1560	GTGGCTGGTCACCCAAAGCT SEQ.ID.IN:326	-13.8	-28.8	78.8	-13	-2	-6.7
59	CCGGGAGGGCCGGGCTGCTC SEQ.ID.IN:327	-13.7	-35	89	-17.6	-3.7	-13.8
554	AAGGAACATCAAGTCCCCAG SEQ.ID.IN:328	-13.7	-24	67.2	-9.4	-0.8	-3.9
703	CTTCGTGCAGGAATCCAAGG SEQ.ID.IN:329	-13.7	-24.6	69	-9.8	-0.3	-10.1
863	TCAGATGATCATTAGGTTTG SEQ.ID.IN:330	-13.7	-19.8	62	-5.4	0	-8.7
1744	TTTTTTGGCAGACACTTCCA SEQ.ID.IN:331	-13.7	-24	70	-10.3	0	-4
828	GTCTCCCTTCTCTCTTTTCA SEQ.ID.IN:332	-13.6	-27.2	81.5	-13.6	0	0
1040	GAACCCGGGAGGCGGAGGCT SEQ.ID.IN:333	-13.6	-31.4	80.1	-15.2	-2.4	-12.6
1421	CAAAGCCAACGGCAAGGGAA SEQ.ID.IN:334	-13.6	-23.4	63.2	-7.3	-2.5	-7.6
1566	CTTTGAGTGGCTGGTCACCC SEQ.ID.IN:335	-13.6	-28.5	80.5	-13.3	-1.5	-7.9
1567	CCTTTGAGTGGCTGGTCACC SEQ.ID.IN:336	-13.6	-28.5	80.5	-13.3	-1.5	-7.9
1710	ATCACACATCTCAGGTCACG SEQ.ID.IN:337	-13.6	-23.8	69.6	-10.2	0	-3
1762	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:338	-13.6	-15.9	53.7	-2.3	0	0
376	CTTCCCCAGGTAGGCCACGG SEQ.ID.IN:339	-13.5	-32.1	83.6	-17.3	-1.2	-7.7
706	CCACTTCGTGCAGGAATCCA SEQ.ID.IN:340	-13.5	-27	73.6	-12.3	-0.5	-10.1
948	ATACAGATGGCCAGGCTTGC SEQ.ID.IN:341	-13.5	-26.7	75.5	-12.3	-0.4	-9.1
1019	CAGTGAGCCAGATTGTACCA SEQ.ID.IN:342	-13.5	-25.5	72.9	-12	0	-4.2
1569	TTCCTTTGAGTGGCTGGTCA SEQ.ID.IN:343	-13.5	-26.8	78.5	-13.3	0	-5.5
50	CCGGGCTGCTCATCACCAGG SEQ.ID.IN:344	-13.4	-30.9	82	-16.5	-0.9	-7.8
140	TCTTCCGCAGCCTCACTTGG SEQ.ID.IN:345	-13.4	-29.3	80.4	-15.9	0	-3.9
256	GTAGATGGTCTCCATGTCGT SEQ.ID.IN:346	-13.4	-25.9	76.2	-10.9	-1.6	-6.5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	AAAGGAGTAGACGAAGCCCA						
289	SEQ.ID.IN:347	-13.4	-23.3	65	-9.9	0	-3.5
	TGTCTTGAAATGGTTCCCAT						
729	SEQ.ID.IN:348	-13.4	-23.4	67.5	-8.6	-1.3	-5.7
	TGGGAATCTTAAATAGAGTC						
845	SEQ.ID.IN:349	-13.4	-17.9	56.6	-3.1	-1.3	-4.3
	GTCATCCCAGCACTTTGGGA						
1215	SEQ.ID.IN:350	-13.4	-28.2	79.3	-11.6	-3.2	-9.6
	ACTCCAGATGGTGGCTGAGC						
1251	SEQ.ID.IN:351	-13.4	-27.5	78.7	-13	-1	-5.5
	GAGCCTTTTAAAACTCCAGA						
1263	SEQ.ID.IN:352	-13.4	-22	63.7	-8.6	0	-7
	ACACACACACACACACACAC						
1659	SEQ.ID.IN:353	-13.4	-22.3	64.2	-8.9	0	0
	ACACACACACACACACACAC						
1669	SEQ.ID.IN:354	-13.4	-22.3	64.2	-8.9	0	0
	GGGAGGGCCGGGCTGCTCAT						
57	SEQ.ID.IN:355	-13.3	-32.9	87.5	-17.6	-1.6	-11.9
	GGTTGGCAAAGGCCTTCTTC						
155	SEQ.ID.IN:356	-13.3	-26.6	75.9	-10.3	-3	-10.6
	GAAAGGAGTAGACGAAGCCC						
290	SEQ.ID.IN:357	-13.3	-23.2	65.1	-9.9	0	-3.5
	ATCAGCTGCTGGTCACAGGT						
487	SEQ.ID.IN:358	-13.3	-27.3	80.2	-12.3	-1.5	-11
	ATCAAGTCCCCAGGTATAGC						
547	SEQ.ID.IN:359	-13.3	-26.3	75	-13	0	-3.3
	CAGTGATTCATGCCTGTCAT						
1230	SEQ.ID.IN:360	-13.3	-24.7	72.3	-11.4	0	-4.5
	TTAAAACTCCAGATGGTGGC						
1256	SEQ.ID.IN:361	-13.3	-21.9	63.8	-7.5	-1	-5.5
	AAAGACATCCAAAGCCAACG						
1430	SEQ.ID.IN:362	-13.3	-20.6	58.1	-7.3	0	-3.2
	AAGTCCCCAGGTATAGCCAC						
544	SEQ.ID.IN:363	-13.2	-28.1	77.5	-13.7	-1.1	-4.6
	AGAGTCTCCCTTCTCTCTTT						
831	SEQ.ID.IN:364	-13.2	-26.6	80.2	-12.4	-0.9	-5
	CAAAGACATCCAAAGCCAAC						
1431	SEQ.ID.IN:365	-13.2	-20.5	58.7	-7.3	0	-3.2
	TTGCAGTTTCCAAACCTTGA						
1611	SEQ.ID.IN:366	-13.2	-23.5	67.2	-10.3	0	-5.3
	TCAAGGGGACATTTGCAGTT						
1623	SEQ.ID.IN:367	-13.2	-23.5	69.1	-10.3	0	-5.2
	AGTCCCCAGGTATAGCCACG						
543	SEQ.ID.IN:368	-13.1	-29.6	79.6	-15.3	-1.1	-4.6
	CTCCCTTCTCTCTTTTCACT						
826	SEQ.ID.IN:369	-13.1	-26.7	78.5	-13.6	0	0
	TTCAGATGATCATTAGGTTT						
864	SEQ.ID.IN:370	-13.1	-19.9	62.4	-6.3	0	-8.1
	CCTGAGCCAGAGAGAAGACT						
1455	SEQ.ID.IN:371	-13.1	-24.8	70.4	-11.1	-0.3	-6.2
	CATTTGCAGTTTCCAAACCT						
1614	SEQ.ID.IN:372	-13.1	-23.6	67.2	-9.7	-0.6	-5.3
	ATCAAGGGGACATTTGCAGT						
1624	SEQ.ID.IN:373	-13.1	-23.4	68.7	-10.3	0	-5.2
	TTTTTGGCAGACACTTCCAT						
1743	SEQ.ID.IN:374	-13.1	-23.9	69.6	-10.3	-0.2	-4
	TTTTTTTGGCAGACACTTCC						
1745	SEQ.ID.IN:375	-13.1	-23.4	69.2	-10.3	0	-4

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1768	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:376	-13.1	-15.9	53.7	-2.8	0	0
47	GGCTGCTCATCACCAGGCTG SEQ.ID.IN:377	-13	-29.6	82.7	-16	-0.3	-6.1
325	GAAGTGCATCCAGGCGACAA SEQ.ID.IN:378	-13	-25.3	69.8	-11.4	-0.8	-5.4
410	GGGTGTAGGTCACGGAGCGG SEQ.ID.IN:379	-13	-28.6	79.5	-13.4	-2.2	-7.5
704	ACTTCGTGCAGGAATCCAAG SEQ.ID.IN:380	-13	-23.6	67.1	-9.5	-0.3	-10.1
715	TCCCATCAGCCACTTCGTGC SEQ.ID.IN:381	-13	-30.1	81.6	-16.6	-0.2	-3.8
717	GTTCCCATCAGCCACTTCGT SEQ.ID.IN:382	-13	-29.6	81.4	-16.6	0	-3.2
985	GGGCAACAGAGCAAGACTCT SEQ.ID.IN:383	-13	-24.5	70.3	-9.8	-1.7	-7.3
1018	AGTGAGCCAGATTGTACCAC SEQ.ID.IN:384	-13	-25	72.4	-12	0	-4.2
1354	TTCCACCATACAGGAACCCA SEQ.ID.IN:385	-13	-26.7	71.7	-12.5	-1.1	-5.8
1464	CCACCCACACCTGAGCCAGA SEQ.ID.IN:386	-13	-31.3	80.6	-17.7	-0.3	-6.2
1739	TGGCAGACACTTCCATTTAA SEQ.ID.IN:387	-13	-22.7	66.1	-9.7	0	-4
101	CGTACATCTTGATGACCAGC SEQ.ID.IN:388	-12.9	-23.9	68.4	-9.2	-1.8	-7.4
823	CCTTCTCTCTTTTCACTGTT SEQ.ID.IN:389	-12.9	-24.7	74.6	-11.8	0	-2.7
104	CCACGTACATCTTGATGACC SEQ.ID.IN:390	-12.8	-24.3	68.2	-9.7	-1.8	-9.6
199	GCTCCTGCAATACTGGGGGC SEQ.ID.IN:391	-12.8	-29.2	80.4	-15.5	-0.8	-6.2
285	GAGTAGACGAAGCCCAGGAA SEQ.ID.IN:392	-12.8	-24.6	68.3	-11.8	0	-3.5
488	CATCAGCTGCTGGTCACAGG SEQ.ID.IN:393	-12.8	-26.8	77.6	-12.3	-1.5	-11
810	CACTGTTAGGGAGGGAGAGG SEQ.ID.IN:394	-12.8	-24.6	72.4	-11.8	0	-2.7
986	TGGGCAACAGAGCAAGACTC SEQ.ID.IN:395	-12.8	-23.6	68.2	-9.8	-0.9	-5.8
1237	CTGAGCACAGTGATTCATGC SEQ.ID.IN:396	-12.8	-23.7	70.2	-10	-0.7	-7.2
1261	GCCTTTTAAAACTCCAGATG SEQ.ID.IN:397	-12.8	-21.4	62.1	-8.6	0	-6.2
1262	AGCCTTTTAAAACTCCAGAT SEQ.ID.IN:398	-12.8	-21.4	62.4	-8.6	0	-6.2
1330	CCCAGCCTTGCTTCCACAGA SEQ.ID.IN:399	-12.8	-30.9	82.4	-17.4	-0.5	-4.2
1453	TGAGCCAGAGAGAAGACTGC SEQ.ID.IN:400	-12.8	-23.7	68.9	-10.9	0.2	-4
40	CATCACCAGGCTGTGGGCAG SEQ.ID.IN:401	-12.7	-28.7	80	-14.4	-1.5	-6.8
713	CCATCAGCCACTTCGTGCAG SEQ.ID.IN:402	-12.7	-28.4	77.8	-14.8	-0.7	-5.3
1761	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:403	-12.7	-15.9	53.7	-3.2	0	0
251	TGGTCTCCATGTCGTTCCGG SEQ.ID.IN:404	-12.6	-28.9	79.7	-15.8	-0.2	-6.3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
705	CACTTCGTGCAGGAATCCAA SEQ.ID.IN:405	-12.6	-24.3	68	-10.6	-0.3	-10.1
827	TCTCCCTTCTCTCTTTTCAC SEQ.ID.IN:406	-12.6	-26.2	78.3	-13.6	0	0
832	TAGAGTCTCCCTTCTCTCTT SEQ.ID.IN:407	-12.6	-26.2	79.1	-12.4	-1.1	-5.5
1012	CCAGATTGTACCACTTCACT SEQ.ID.IN:408	-12.6	-24.6	70.6	-12	0	-4.2
1232	CACAGTGATTCATGCCTGTC SEQ.ID.IN:409	-12.6	-24.9	73	-11.4	-0.8	-7.2
1355	CTTCCACCATACAGGAACCC SEQ.ID.IN:410	-12.6	-26.9	72.5	-12.9	-1.3	-5.8
1366	GGCTCACCCAGCTTCCACCA SEQ.ID.IN:411	-12.6	-32.7	86.4	-18.3	-1.8	-4.8
1448	CAGAGAGAAGACTGCAGCAA SEQ.ID.IN:412	-12.6	-21.8	64.2	-8.5	0	-8.9
1452	GAGCCAGAGAGAAGACTGCA SEQ.ID.IN:413	-12.6	-24.4	70.2	-10.9	-0.8	-4.7
1709	TCACACATCTCAGGTCACGG SEQ.ID.IN:414	-12.6	-25	72.3	-12.4	0	-3.5
56	GGAGGGCCGGGCTGCTCATC SEQ.ID.IN:415	-12.5	-32.1	86.8	-17.6	-1.6	-11.9
144	GCCTTCTTCCGCAGCCTCAC SEQ.ID.IN:416	-12.5	-31.9	85.9	-19.4	0	-3.9
264	AGGAAGGGGTAGATGGTCTC SEQ.ID.IN:417	-12.5	-24.3	73	-11.8	0	-2.8
335	GGAAGACCAGGAAGTGCATC SEQ.ID.IN:418	-12.5	-23.8	68.6	-10.6	-0.5	-6.4
396	GAGCGGATGGGTGCCCGCAG SEQ.ID.IN:419	-12.5	-31.7	82	-14.6	-4.6	-10.7
833	ATAGAGTCTCCCTTCTCTCT SEQ.ID.IN:420	-12.5	-26.1	78.6	-12.4	-1.1	-5.5
897	TCAGTCTGAAAAGTCTGCAT SEQ.ID.IN:421	-12.5	-21.1	64	-8.1	-0.1	-5.1
987	TTGGGCAACAGAGCAAGACT SEQ.ID.IN:422	-12.5	-23.3	67.1	-9.8	-0.9	-5.2
1216	TGTCATCCCAGCACTTTGGG SEQ.ID.IN:423	-12.5	-27.6	77.7	-13.1	-2	-7.2
1266	TGGGAGCCTTTTAAAACTCC SEQ.ID.IN:424	-12.5	-23.1	65.8	-8.6	-1.8	-11.4
1571	AGTTCCTTTGAGTGGCTGGT SEQ.ID.IN:425	-12.5	-26.9	79.6	-14.4	0	-4
1621	AAGGGGACATTTGCAGTTTC SEQ.ID.IN:426	-12.5	-22.9	68.3	-10.4	0	-5.2
1758	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:427	-12.5	-15.9	53.7	-3.4	0	0
54	AGGGCCGGGCTGCTCATCAC SEQ.ID.IN:428	-12.4	-31.2	84.5	-17.6	-0.8	-9.8
55	GAGGGCCGGGCTGCTCATCA SEQ.ID.IN:429	-12.4	-31.6	85.2	-17.6	-0.8	-11.3
557	TGGAAGGAACATCAAGTCCC SEQ.ID.IN:430	-12.4	-23.1	65.9	-10.2	-0.1	-5.1
733	AATCTGTCTTGAAATGGTTC SEQ.ID.IN:431	-12.4	-19.3	60	-6.4	-0.1	-2.7
1568	TCCTTTGAGTGGCTGGTCAC SEQ.ID.IN:432	-12.4	-26.9	78.8	-13.3	-1.1	-7.5
1757	TTTTTTTTTTTTTTTTTTTG SEQ.ID.IN:433	-12.4	-15.8	53.3	-3.4	0	0

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
61	GGCCGGGAGGGCCGGGCTGC SEQ.ID.IN:434	-12.3	-36.7	91.9	-19.3	-5.1	-15
141	TTCTTCCGCAGCCTCACTTG SEQ.ID.IN:435	-12.3	-28.2	78.3	-15.9	0	-3.9
1265	GGGAGCCTTTTAAAACTCCA SEQ.ID.IN:436	-12.3	-23.8	67	-8.6	-2.9	-12.6
1467	CTCCCACCCACACCTGAGCC SEQ.ID.IN:437	-12.3	-33.3	84.7	-21	0	-3.2
1473	GGGCCCCTCCCACCCACACC SEQ.ID.IN:438	-12.3	-38.2	92.3	-24	-1.9	-9.2
1740	TTGGCAGACACTTCCATTTA SEQ.ID.IN:439	-12.3	-23.5	68.7	-10.7	-0.2	-4
158	CGGGGTTGGCAAAGGCCTTC SEQ.ID.IN:440	-12.2	-28.4	76.7	-13.2	-3	-10.6
483	GCTGCTGGTCACAGGTGGCG SEQ.ID.IN:441	-12.2	-30	83.5	-15.9	-1.9	-7.3
806	GTTAGGGAGGGAGAGGGAGT SEQ.ID.IN:442	-12.2	-25.8	76.9	-13.6	0	-0.6
1703	ATCTCAGGTCACGGGTCTAG SEQ.ID.IN:443	-12.2	-25.5	75.6	-13.3	0	-3.5
1767	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:444	-12.2	-15.9	53.7	-3.7	0	0
139	CTTCCGCAGCCTCACTTGGC SEQ.ID.IN:445	-12.1	-30.7	83	-17	-1.5	-5.8
185	GGGGGCCTCCGTGTCTCAGG SEQ.ID.IN:446	-12.1	-32.7	89.4	-19	-1.1	-11
486	TCAGCTGCTGGTCACAGGTG SEQ.ID.IN:447	-12.1	-27.3	80	-12.3	-2.9	-11
753	GATTTTCTATCAATCTTCAC SEQ.ID.IN:448	-12.1	-19	60.2	-6.4	-0.1	-3.5
1222	CATGCCTGTCATCCCAGCAC SEQ.ID.IN:449	-12.1	-29.5	80.6	-16.5	-0.7	-4.5
1283	CATCACAGGGACTCACATGG SEQ.ID.IN:450	-12.1	-24	69.5	-11.3	-0.3	-5.6
1365	GCTCACCCAGCTTCCACCAT SEQ.ID.IN:451	-12.1	-31.5	83.9	-18.3	-1	-4.5
328	CAGGAAGTGCATCCAGGCGA SEQ.ID.IN:452	-12	-27	74.2	-13.4	-1.5	-8.7
337	GAGGAAGACCAGGAAGTGCA SEQ.ID.IN:453	-12	-24	68.6	-10.6	-1.3	-6.9
385	TGCCCGCAGCTTCCCCAGGT SEQ.ID.IN:454	-12	-35.4	90	-22.3	-1	-4.8
719	TGGTTCCCATCAGCCACTTC SEQ.ID.IN:455	-12	-28.8	80.7	-16.1	-0.5	-3.8
1062	GGCTGAGGCGGGAGAATCGC SEQ.ID.IN:456	-12	-28.2	76.1	-13.8	-2.4	-8
1267	ATGGGAGCCTTTTAAAACTC SEQ.ID.IN:457	-12	-21.1	62.2	-8.6	0	-7.8
1353	TCCACCATACAGGAACCCAA SEQ.ID.IN:458	-12	-25.9	69.3	-13.1	-0.6	-4.8
1572	AAGTTCCTTTGAGTGGCTGG SEQ.ID.IN:459	-12	-25	73.2	-13	0	-4
252	ATGGTCTCCATGTCGTTCCG SEQ.ID.IN:460	-11.9	-27.7	77.1	-14.7	-1	-5.7
541	TCCCCAGGTATAGCCACGGC SEQ.ID.IN:461	-11.9	-31.4	82.6	-18.3	-1.1	-6.9
844	GGGAATCTTAAATAGAGTCT SEQ.ID.IN:462	-11.9	-18.8	58.6	-4.8	-2.1	-5.1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1056	GGCGGGAGAATCGCTTGAAC SEQ.ID.IN:463	-11.9	-24.8	68.2	-10	-2.9	-7.5
1210	CCCAGCACTTTGGGAGGCCG SEQ.ID.IN:464	-11.9	-31.3	81.4	-17.2	-1.8	-12.2
1320	CTTCCACAGAGAACTGGCAG SEQ.ID.IN:465	-11.9	-24.3	69.7	-10.7	-1.7	-6.8
1367	TGGCTCACCCAGCTTCCACC SEQ.ID.IN:466	-11.9	-32	85.3	-18.3	-1.8	-6
1472	GGCCCCTCCCACCCACACCT SEQ.ID.IN:467	-11.9	-37.9	91.7	-26	0	-5.6
1561	AGTGGCTGGTCACCCAAAGC SEQ.ID.IN:468	-11.9	-27.9	77.3	-14.4	-1.5	-7.9
1609	GCAGTTTCCAAACCTTGAAG SEQ.ID.IN:469	-11.9	-22.7	65.1	-10.3	-0.2	-5.3
1610	TGCAGTTTCCAAACCTTGAA SEQ.ID.IN:470	-11.9	-22.7	64.8	-10.3	-0.2	-5.3
1738	GGCAGACACTTCCATTTAAT SEQ.ID.IN:471	-11.9	-22.7	66.2	-10.8	0	-4
535	GGTATAGCCACGGCGGCTCT SEQ.ID.IN:472	-11.8	-30.3	81.2	-15.7	-2.8	-10.9
716	TTCCCATCAGCCACTTCGTG SEQ.ID.IN:473	-11.8	-28.4	77.7	-16.6	0	-3.8
801	GGAGGGAGAGGGAGTGATGT SEQ.ID.IN:474	-11.8	-25.4	75	-13.6	0	-1.1
802	GGGAGGGAGAGGGAGTGATG SEQ.ID.IN:475	-11.8	-25.4	74.1	-13.6	0	-1.1
803	AGGGAGGGAGAGGGAGTGAT SEQ.ID.IN:476	-11.8	-25.4	74.6	-13.6	0	-1.1
900	GGGTCAGTCTGAAAAGTCTG SEQ.ID.IN:477	-11.8	-22.2	67.1	-9.7	-0.4	-6.4
1257	TTTAAAACTCCAGATGGTGG SEQ.ID.IN:478	-11.8	-20.2	60.2	-7.5	-0.8	-5.6
1562	GAGTGGCTGGTCACCCAAAG SEQ.ID.IN:479	-11.8	-26.7	74.3	-13.3	-1.5	-7.9
1565	TTTGAGTGGCTGGTCACCCA SEQ.ID.IN:480	-11.8	-28.3	79.6	-15.6	-0.8	-7.1
1613	ATTTGCAGTTTCCAAACCTT SEQ.ID.IN:481	-11.8	-23	66.4	-10.4	-0.6	-5.3
1654	CACACACACACACACACACA SEQ.ID.IN:482	-11.8	-22.8	64.8	-11	0	0
1656	CACACACACACACACACACA SEQ.ID.IN:483	-11.8	-22.8	64.8	-11	0	0
1672	CACACACACACACACACACA SEQ.ID.IN:484	-11.8	-22.8	64.8	-11	0	0
1674	CACACACACACACACACACA SEQ.ID.IN:485	-11.8	-22.8	64.8	-11	0	0
1741	TTTGGCAGACACTTCCATTT SEQ.ID.IN:486	-11.8	-23.9	69.6	-11.6	-0.2	-4
1760	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:487	-11.8	-15.9	53.7	-4.1	0	0
323	AGTGCATCCAGGCGACAAAA SEQ.ID.IN:488	-11.7	-24	66.5	-11.4	-0.8	-5.4
324	AAGTGCATCCAGGCGACAAA SEQ.ID.IN:489	-11.7	-24	66.5	-11.4	-0.8	-5.4
498	GCCAAGGAGGCATCAGCTGC SEQ.ID.IN:490	-11.7	-28.9	80.3	-14.3	-2.6	-13.5
947	TACAGATGGCCAGGCTTGCC SEQ.ID.IN:491	-11.7	-28.7	79.1	-15.6	-1.2	-9.9

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1020	GCAGTGAGCCAGATTGTACC SEQ.ID.IN:492	-11.7	-26.6	76.2	-14.4	-0.1	-4.4
1264	GGAGCCTTTTAAAACTCCAG SEQ.ID.IN:493	-11.7	-22.6	64.9	-8.6	-2.1	-12
1274	GACTCACATGGGAGCCTTTT SEQ.ID.IN:494	-11.7	-25.7	73.6	-13.3	-0.4	-8.1
1456	ACCTGAGCCAGAGAGAAGAC SEQ.ID.IN:495	-11.7	-24.1	69.1	-11.8	-0.3	-6.2
250	GGTCTCCATGTCGTTCCGGT SEQ.ID.IN:496	-11.6	-30.1	83.5	-18.5	0	-6.6
261	AAGGGGTAGATGGTCTCCAT SEQ.ID.IN:497	-11.6	-25.2	73.5	-12.1	-1.4	-6.5
334	GAAGACCAGGAAGTGCATCC SEQ.ID.IN:498	-11.6	-24.6	69.6	-12.3	-0.4	-7.4
914	GGCCAGAATTTCTGGGGTCA SEQ.ID.IN:499	-11.6	-27	76.7	-11.8	-3.6	-13.5
1258	TTTTAAAACTCCAGATGGTG SEQ.ID.IN:500	-11.6	-19.1	58.1	-7.5	0	-6
1474	TGGGCCCCTCCCACCCACAC SEQ.ID.IN:501	-11.6	-36.2	89.1	-22	-2.6	-10.2
142	CTTCTTCCGCAGCCTCACTT SEQ.ID.IN:502	-11.5	-29.1	80.4	-17.6	0	-3.9
150	GCAAAGGCCTTCTTCCGCAG SEQ.ID.IN:503	-11.5	-28.2	76.1	-15.2	-1	-10.6
191	AATACTGGGGGCCTCCGTGT SEQ.ID.IN:504	-11.5	-29.2	78.8	-15.8	-1.1	-11.8
301	GTTAGGACCCAGAAAGGAGT SEQ.ID.IN:505	-11.5	-23.9	68.8	-11.9	-0.2	-4.1
389	TGGGTGCCCGCAGCTTCCCC SEQ.ID.IN:506	-11.5	-35.9	90.9	-21.5	-2.9	-9.7
711	ATCAGCCACTTCGTGCAGGA SEQ.ID.IN:507	-11.5	-27.5	77.1	-15.1	-0.7	-8
804	TAGGGAGGGAGAGGGAGTGA SEQ.ID.IN:508	-11.5	-25.1	74	-13.6	0	-0.2
1359	CCAGCTTCCACCATACAGGA SEQ.ID.IN:509	-11.5	-27.9	76.2	-15.6	-0.6	-6
1443	AGAAGACTGCAGCAAAGACA SEQ.ID.IN:510	-11.5	-20.7	61.2	-8.5	0	-8.9
162	TCCTCGGGGTTGGCAAAGGC SEQ.ID.IN:511	-11.4	-28.7	78	-16.4	-0.7	-8
167	GGGCATCCTCGGGGTTGGCA SEQ.ID.IN:512	-11.4	-32	86.3	-19.1	-1.4	-8.4
336	AGGAAGACCAGGAAGTGCAT SEQ.ID.IN:513	-11.4	-23.4	67.3	-10.6	-1.3	-7.1
379	CAGCTTCCCCAGGTAGGCCA SEQ.ID.IN:514	-11.4	-32.4	86.8	-19.7	-1.2	-7.7
1066	AGGAGGCTGAGGCGGGAGAA SEQ.ID.IN:515	-11.4	-27	75	-14.7	-0.8	-4
1432	GCAAAGACATCCAAAGCCAA SEQ.ID.IN:516	-11.4	-22.1	61.8	-10.7	0	-3.5
1444	GAGAAGACTGCAGCAAAGAC SEQ.ID.IN:517	-11.4	-20.6	61.3	-8.5	0	-8.9
1483	AGCTTCCTGTGGGCCCCTCC SEQ.ID.IN:518	-11.4	-34.8	92.4	-22.2	0	-10.3
1625	CATCAAGGGGACATTTGCAG SEQ.ID.IN:519	-11.4	-22.9	66.6	-11.5	0	-5.2
106	CACCACGTACATCTTGATGA SEQ.ID.IN:520	-11.3	-23	65.8	-9.9	-1.8	-9.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	TGGCCACCACGTACATCTTG						
110	SEQ.ID.IN:521	-11.3	-26.8	73.2	-14.9	-0.2	-8.3
	GATGGCCACCACGTACATCT						
112	SEQ.ID.IN:522	-11.3	-27.3	74.3	-14.9	-1	-9.1
	AGGGCATCCTCGGGGTTGGC						
168	SEQ.ID.IN:523	-11.3	-31.3	85.8	-19.1	-0.8	-7.7
	CTGGGGGCCTCCGTGTCTCA						
187	SEQ.ID.IN:524	-11.3	-32.4	88	-19	-1.1	-12.2
	GCAGCTTCCCCAGGTAGGCC						
380	SEQ.ID.IN:525	-11.3	-33.5	90.4	-21.7	-0.1	-6.4
	AGCTGCTGGTCACAGGTGGC						
484	SEQ.ID.IN:526	-11.3	-29.2	84.6	-16.3	-1.6	-9
	TGATGCTCTGTTACTTTAGC						
778	SEQ.ID.IN:527	-11.3	-22.4	68.5	-10.5	-0.3	-3.7
	GGTCAGTCTGAAAAGTCTGC						
899	SEQ.ID.IN:528	-11.3	-22.8	68.8	-10.8	-0.4	-6.5
	CGGGAGAATCGCTTGAACCC						
1054	SEQ.ID.IN:529	-11.3	-25.8	68.7	-13.6	-0.8	-5.2
	GACTGCAGCAAAGACATCCA						
1439	SEQ.ID.IN:530	-11.3	-23.9	67.7	-11.9	0	-8.9
	ACACACACACACACACACGG						
1651	SEQ.ID.IN:531	-11.3	-23.4	65.2	-12.1	0	-3.5
	ACACACACACACACACACAC						
1655	SEQ.ID.IN:532	-11.3	-22.3	64.2	-11	0	0
	ACACACACACACACACACAC						
1673	SEQ.ID.IN:533	-11.3	-22.3	64.2	-11	0	0
	CAGGCTGTGGGCAGGCATCT						
34	SEQ.ID.IN:534	-11.2	-29.7	84	-16.9	-1.5	-5.5
	GATGGTCTCCATGTCGTTCC						
253	SEQ.ID.IN:535	-11.2	-27.5	78.8	-14.7	-1.6	-6.5
	GCCCGCAGCTTCCCCAGGTA						
384	SEQ.ID.IN:536	-11.2	-35.1	89.7	-23.3	-0.3	-4.5
	ATGGTTCCCATCAGCCACTT						
720	SEQ.ID.IN:537	-11.2	-28.4	78.8	-16.1	-1	-5.2
	AGTCTCCCTTCTCTCTTTTC						
829	SEQ.ID.IN:538	-11.2	-26.5	80.8	-15.3	0	-1.5
	GAGCAAGACTCTGTCTTGGA						
977	SEQ.ID.IN:539	-11.2	-23.8	70.9	-8.4	-4.2	-12
	CAGCAAAGACATCCAAAGCC						
1434	SEQ.ID.IN:540	-11.2	-22.8	63.8	-11.6	0	-4.1
	AGAGAAGACTGCAGCAAAGA						
1445	SEQ.ID.IN:541	-11.2	-20.4	60.9	-8.5	0	-8.9
	GAGAGAAGACTGCAGCAAAG						
1446	SEQ.ID.IN:542	-11.2	-20.4	60.9	-8.5	0	-8.9
	AGAGAGAAGACTGCAGCAAA						
1447	SEQ.ID.IN:543	-11.2	-20.4	60.9	-8.5	0	-8.9
	TTTTTTTTGGCAGACACTTC						
1746	SEQ.ID.IN:544	-11.2	-21.5	65.7	-10.3	0	-4
	GCCGGGAGGGCCGGGCTGCT						
60	SEQ.ID.IN:545	-11.1	-36.4	91.3	-20.9	-4.4	-14.3
	ACTGGGGGCCTCCGTGTCTC						
188	SEQ.ID.IN:546	-11.1	-31.9	87.7	-19	-1	-11.6
	GGTTAGGACCCAGAAAGGAG						
302	SEQ.ID.IN:547	-11.1	-23.9	68.1	-11.9	-0.8	-4.2
	CGACAAAAGGGTTAGGACCC						
311	SEQ.ID.IN:548	-11.1	-23.6	65.1	-9.5	-3	-8
	CAGGGCCCACCACAATCTGG						
574	SEQ.ID.IN:549	-11.1	-29.2	77.2	-15.7	-1.3	-12.9

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
755	AGGATTTTCTATCAATCTTC SEQ.ID.IN:550	-11.1	-19.3	61.2	-7.2	-0.9	-4.4
865	ATTCAGATGATCATTAGGTT SEQ.ID.IN:551	-11.1	-19.8	62.1	-8	0	-8.7
896	CAGTCTGAAAAGTCTGCATT SEQ.ID.IN:552	-11.1	-20.8	62.9	-9	-0.4	-5.7
979	CAGAGCAAGACTCTGTCTTG SEQ.ID.IN:553	-11.1	-22.7	68.3	-8.4	-3.2	-10.6
1229	AGTGATTCATGCCTGTCATC SEQ.ID.IN:554	-11.1	-24.4	72.9	-13.3	0	-4.4
1364	CTCACCCAGCTTCCACCATA SEQ.ID.IN:555	-11.1	-29.4	79.1	-18.3	0	-4.5
1564	TTGAGTGGCTGGTCACCCAA SEQ.ID.IN:556	-11.1	-27.5	76.6	-14.8	-1.5	-8
1715	TAAAAATCACACATCTCAGG SEQ.ID.IN:557	-11.1	-17.4	54.3	-6.3	0	-1.7
1755	TTTTTTTTTTTTTTTTTGGC SEQ.ID.IN:558	-11.1	-18.6	59.7	-7.5	0	-2.8
32	GGCTGTGGGCAGGCATCTCT SEQ.ID.IN:559	-11	-30.3	86.7	-17.7	-1.5	-5.5
51	GCCGGGCTGCTCATCACCAG SEQ.ID.IN:560	-11	-31.5	83.8	-19.5	-0.9	-8.9
111	ATGGCCACCACGTACATCTT SEQ.ID.IN:561	-11	-26.8	73.4	-14.9	-0.6	-9.1
575	TCAGGGCCCACCACAATCTG SEQ.ID.IN:562	-11	-28.4	76.4	-15.7	-1.3	-11.3
732	ATCTGTCTTGAAATGGTTCC SEQ.ID.IN:563	-11	-22	66.1	-10.3	-0.5	-3
805	TTAGGGAGGGAGAGGGAGTG SEQ.ID.IN:564	-11	-24.6	73	-13.6	0	-0.6
807	TGTTAGGGAGGGAGAGGGAG SEQ.ID.IN:565	-11	-24.6	73	-13.6	0	-0.6
957	AAAAAAAAAATACAGATGGC SEQ.ID.IN:566	-11	-11.9	42.7	-0.7	0	-2.8
1011	CAGATTGTACCACTTCACTC SEQ.ID.IN:567	-11	-23	68.5	-12	0	-4.2
1039	AACCCGGGAGGCGGAGGCTG SEQ.ID.IN:568	-11	-30.8	78.8	-17.2	-2.4	-12.6
1463	CACCCACACCTGAGCCAGAG SEQ.ID.IN:569	-11	-29.3	77.7	-17.7	-0.3	-6.2
558	CTGGAAGGAACATCAAGTCC SEQ.ID.IN:570	-10.9	-22	64.2	-10.6	-0.2	-3.7
707	GCCACTTCGTGCAGGAATCC SEQ.ID.IN:571	-10.9	-28.1	76.7	-16.2	-0.2	-9.9
714	CCCATCAGCCACTTCGTGCA SEQ.ID.IN:572	-10.9	-30.4	80.8	-18.6	-0.7	-5.2
1482	GCTTCCTGTGGGCCCCTCCC SEQ.ID.IN:573	-10.9	-36.8	95.1	-24.3	-1.5	-10.3
1542	CTCCCGGTCCTCCACCCACT SEQ.ID.IN:574	-10.9	-34.9	88.1	-23.3	-0.4	-6.2
1759	TTTTTTTTTTTTTTTTTTTT SEQ.ID.IN:575	-10.9	-15.9	53.7	-5	0	0
147	AAGGCCTTCTTCCGCAGCCT SEQ.ID.IN:576	-10.8	-31.1	82.7	-18.2	-2.1	-9.8
255	TAGATGGTCTCCATGTCGTT SEQ.ID.IN:577	-10.8	-24.8	73	-12.4	-1.6	-6.5
297	GGACCCAGAAAGGAGTAGAC SEQ.ID.IN:578	-10.8	-23.4	67.1	-11.9	-0.4	-3.5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
540	CCCCAGGTATAGCCACGGCG SEQ.ID.IN:579	-10.8	-31.8	80.4	-20.1	-0.7	-8.2
904	TCTGGGGTCAGTCTGAAAAG SEQ.ID.IN:580	-10.8	-22.2	66.4	-10.1	-1.2	-6.9
1211	TCCCAGCACTTTGGGAGGCC SEQ.ID.IN:581	-10.8	-30.9	83.7	-17.2	-2.9	-12.8
1214	TCATCCCAGCACTTTGGGAG SEQ.ID.IN:582	-10.8	-27	76.1	-12.8	-3.4	-9.9
1236	TGAGCACAGTGATTCATGCC SEQ.ID.IN:583	-10.8	-24.8	71.9	-12.8	-1.1	-7.6
1417	GCCAACGGCAAGGGAAGCGT SEQ.ID.IN:584	-10.8	-27.9	72.7	-15.4	-1.7	-7.5
1419	AAGCCAACGGCAAGGGAAGC SEQ.ID.IN:585	-10.8	-25.2	67.9	-11.9	-2.5	-7.6
1652	CACACACACACACACACACG SEQ.ID.IN:586	-10.8	-22.9	64	-12.1	0	-3
1716	CTAAAAATCACACATCTCAG SEQ.ID.IN:587	-10.8	-17.1	53.7	-6.3	0	-1.3
1742	TTTTGGCAGACACTTCCATT SEQ.ID.IN:588	-10.8	-23.9	69.6	-12.6	-0.2	-3.5
41	TCATCACCAGGCTGTGGGCA SEQ.ID.IN:589	-10.7	-29.1	81.5	-16.8	-1.5	-6.9
159	TCGGGGTTGGCAAAGGCCTT SEQ.ID.IN:590	-10.7	-28.4	76.7	-14.7	-3	-10.4
306	AAAGGGTTAGGACCCAGAAA SEQ.ID.IN:591	-10.7	-21.9	62.5	-7.1	-4.1	-9.2
702	TTCGTGCAGGAATCCAAGGG SEQ.ID.IN:592	-10.7	-24.9	69.6	-13.2	-0.3	-9.8
800	GAGGGAGAGGGAGTGATGTT SEQ.ID.IN:593	-10.7	-24.3	72.6	-13.6	0	-1.1
824	CCCTTCTCTCTTTTCACTGT SEQ.ID.IN:594	-10.7	-26.6	78	-15.9	0	-2.4
901	GGGGTCAGTCTGAAAAGTCT SEQ.ID.IN:595	-10.7	-23.4	69.9	-12	-0.4	-6.1
1055	GCGGGAGAATCGCTTGAACC SEQ.ID.IN:596	-10.7	-25.6	69.2	-12.8	-2.1	-6.6
1065	GGAGGCTGAGGCGGGAGAAT SEQ.ID.IN:597	-10.7	-27	74.6	-14.7	-1.6	-4.7
1342	GGAACCCAAGACCCCAGCCT SEQ.ID.IN:598	-10.7	-31.5	79.1	-20.8	0	-3.2
1608	CAGTTTCCAAACCTTGAAGA SEQ.ID.IN:599	-10.7	-21.5	62.5	-10.3	-0.2	-5.3
1676	CACACACACACACACACACA SEQ.ID.IN:600	-10.7	-22.8	64.8	-12.1	0	0
1714	AAAAATCACACATCTCAGGT SEQ.ID.IN:601	-10.7	-18.9	57.7	-8.2	0	-2.5
203	GGTCGCTCCTGCAATACTGG SEQ.ID.IN:602	-10.6	-27.4	75.8	-15.4	-1.3	-5.2
295	ACCCAGAAAGGAGTAGACGA SEQ.ID.IN:603	-10.6	-23	64.9	-11.9	-0.2	-3.7
298	AGGACCCAGAAAGGAGTAGA SEQ.ID.IN:604	-10.6	-23.2	66.8	-11.9	-0.4	-4.1
312	GCGACAAAAGGGTTAGGACC SEQ.ID.IN:605	-10.6	-23.4	65.5	-11.5	-1.2	-5.8
368	GGTAGGCCACGGTGTGTGCC SEQ.ID.IN:606	-10.6	-31.4	85.8	-17.6	-3.2	-10.6
573	AGGGCCCACCACAATCTGGA SEQ.ID.IN:607	-10.6	-29.1	77.4	-15.7	-1.3	-13.7

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
978	AGAGCAAGACTCTGTCTTGG SEQ.ID.IN:608	-10.6	-23.2	69.8	-8.4	-4.2	-12
984	GGCAACAGAGCAAGACTCTG SEQ.ID.IN:609	-10.6	-23.3	67.6	-9.8	-2.9	-11.6
1225	ATTCATGCCTGTCATCCCAG SEQ.ID.IN:610	-10.6	-27.3	76.7	-16.7	0	-4.4
1433	AGCAAAGACATCCAAAGCCA SEQ.ID.IN:611	-10.6	-22.8	63.8	-12.2	0	-4.1
1440	AGACTGCAGCAAAGACATCC SEQ.ID.IN:612	-10.6	-23.2	66.8	-11.9	0	-8.9
1653	ACACACACACACACACACAC SEQ.ID.IN:613	-10.6	-22.3	64.2	-11.7	0	0
1675	ACACACACACACACACACAC SEQ.ID.IN:614	-10.6	-22.3	64.2	-11.7	0	0
1719	TGACTAAAAATCACACATCT SEQ.ID.IN:615	-10.6	-16.8	52.9	-6.2	0	-2.7
1754	TTTTTTTTTTTTTTTTGGCA SEQ.ID.IN:616	-10.6	-19.2	60.6	-8.6	0	-4
67	CAGGAAGGCCGGGAGGGCCG SEQ.ID.IN:617	-10.5	-31.6	80.2	-16	-5.1	-10.8
300	TTAGGACCCAGAAAGGAGTA SEQ.ID.IN:618	-10.5	-22.4	65.1	-11.9	0.2	-4.1
322	GTGCATCCAGGCGACAAAAG SEQ.ID.IN:619	-10.5	-24	66.5	-12.6	-0.7	-5.4
371	CCAGGTAGGCCACGGTGTGT SEQ.ID.IN:620	-10.5	-30.3	83	-18.5	-1.2	-7.7
489	GCATCAGCTGCTGGTCACAG SEQ.ID.IN:621	-10.5	-27.4	79.5	-15.1	-1.7	-11
728	GTCTTGAAATGGTTCCCATC SEQ.ID.IN:622	-10.5	-23.8	69.2	-11.7	-1.5	-5.9
956	AAAAAAAAATACAGATGGCC SEQ.ID.IN:623	-10.5	-14.6	47.4	-4.1	0	-6.2
1331	CCCCAGCCTTGCTTCCACAG SEQ.ID.IN:624	-10.5	-32.3	84.4	-21.1	-0.5	-4.2
46	GCTGCTCATCACCAGGCTGT SEQ.ID.IN:625	-10.4	-29.6	83.7	-18.6	-0.3	-5.2
113	TGATGGCCACCACGTACATC SEQ.ID.IN:626	-10.4	-26.4	72.3	-14.9	-0.9	-9.1
186	TGGGGGCCTCCGTGTCTCAG SEQ.ID.IN:627	-10.4	-31.5	86.4	-19	-1.1	-12.2
296	GACCCAGAAAGGAGTAGACG SEQ.ID.IN:628	-10.4	-23	64.9	-11.9	-0.4	-3.5
534	GTATAGCCACGGCGGCTCTT SEQ.ID.IN:629	-10.4	-29.2	79.1	-15.7	-3.1	-10.9
537	CAGGTATAGCCACGGCGGCT SEQ.ID.IN:630	-10.4	-29.7	79	-16.4	-2.9	-10.9
542	GTCCCCAGGTATAGCCACGG SEQ.ID.IN:631	-10.4	-30.8	81.8	-19.2	-1.1	-4.6
1217	CTGTCATCCCAGCACTTTGG SEQ.ID.IN:632	-10.4	-27.3	77.1	-16.4	-0.1	-4.2
1272	CTCACATGGGAGCCTTTTAA SEQ.ID.IN:633	-10.4	-23.9	68.8	-13.5	0	-7.2
1357	AGCTTCCACCATACAGGAAC SEQ.ID.IN:634	-10.4	-24.7	69.9	-12.9	-1.3	-5.8
1471	GCCCCTCCCACCCACACCTG SEQ.ID.IN:635	-10.4	-36.7	89.2	-26.3	0	-2
1708	CACACATCTCAGGTCACGGG SEQ.ID.IN:636	-10.4	-25.8	73.2	-15.4	0	-3.5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
219	CAGCGTTCCACGTCGGGGTC SEQ.ID.IN:637	-10.3	-30.3	81.4	-18.7	-1.2	-8.4
381	CGCAGCTTCCCCAGGTAGGC SEQ.ID.IN:638	-10.3	-32.3	86.2	-22	0	-4.5
1356	GCTTCCACCATACAGGAACC SEQ.ID.IN:639	-10.3	-26.7	73.1	-15	-1.3	-5.8
1374	CTGTCCTTGGCTCACCCAGC SEQ.ID.IN:640	-10.3	-31.2	85.6	-19.8	-1	-5
1543	GCTCCCGGTCCTCCACCCAC SEQ.ID.IN:641	-10.3	-35.8	90.5	-24.5	-0.9	-6.2
70	GAGCAGGAAGGCCGGGAGGG SEQ.ID.IN:642	-10.2	-29.4	78.9	-17.6	-1.5	-7.7
100	GTACATCTTGATGACCAGCA SEQ.ID.IN:643	-10.2	-23.8	69.4	-11.8	-1.8	-7.4
799	AGGGAGAGGGAGTGATGTTT SEQ.ID.IN:644	-10.2	-23.8	71.6	-13.6	0	-1.1
1116	TACAAAAATTAGCTGGGTAT SEQ.ID.IN:645	-10.2	-17.6	54.7	-7.4	0	-4.8
1231	ACAGTGATTCATGCCTGTCA SEQ.ID.IN:646	-10.2	-24.9	73	-13.9	-0.6	-7
1235	GAGCACAGTGATTCATGCCT SEQ.ID.IN:647	-10.2	-25.7	74.1	-14.3	-1.1	-7.6
1252	AACTCCAGATGGTGGCTGAG SEQ.ID.IN:648	-10.2	-25	71.7	-13.7	-1	-5.5
1372	GTCCTTGGCTCACCCAGCTT SEQ.ID.IN:649	-10.2	-31.3	86.3	-19.3	-1.8	-6
1373	TGTCCTTGGCTCACCCAGCT SEQ.ID.IN:650	-10.2	-31.2	85.6	-19.2	-1.8	-5.2
1460	CCACACCTGAGCCAGAGAGA SEQ.ID.IN:651	-10.2	-27.6	75.5	-16.8	-0.3	-6.2
1606	GTTTCCAAACCTTGAAGATA SEQ.ID.IN:652	-10.2	-20.5	60.6	-10.3	0	-4.1
1677	ACACACACACACACACACAC SEQ.ID.IN:653	-10.2	-22.3	64.2	-12.1	0	0
1756	TTTTTTTTTTTTTTTTTTGG SEQ.ID.IN:654	-10.2	-16.9	55.7	-6.7	0	0
377	GCTTCCCCAGGTAGGCCACG SEQ.ID.IN:655	-10.1	-32.7	85.4	-21.3	-1.2	-7.7
1030	GGCGGAGGCTGCAGTGAGCC SEQ.ID.IN:656	-10.1	-31.6	86	-18.7	-2.8	-11.3
1115	ACAAAAATTAGCTGGGTATG SEQ.ID.IN:657	-10.1	-17.9	55.2	-7.8	0	-4.8
1118	AATACAAAAATTAGCTGGGT SEQ.ID.IN:658	-10.1	-17.2	53.5	-7.1	0	-4.8
1346	TACAGGAACCCAAGACCCCA SEQ.ID.IN:659	-10.1	-27.4	71.5	-16.7	-0.3	-3.7
1416	CCAACGGCAAGGGAAGCGTC SEQ.ID.IN:660	-10.1	-26.5	70.4	-15.4	-0.9	-4.9
1559	TGGCTGGTCACCCAAAGCTC SEQ.ID.IN:661	-10.1	-28	77.2	-15.9	-2	-8.1
143	CCTTCTTCCGCAGCCTCACT SEQ.ID.IN:662	-10	-31	83.4	-21	0	-3.9
146	AGGCCTTCTTCCGCAGCCTC SEQ.ID.IN:663	-10	-32.2	87.3	-20.3	-1.9	-7.9
867	GGATTCAGATGATCATTAGG SEQ.ID.IN:664	-10	-20.3	62.5	-9.5	-0.5	-8.7
868	GGGATTCAGATGATCATTAG SEQ.ID.IN:665	-10	-20.3	62.5	-9.5	-0.5	-8.7

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
963	CTTGGAAAAAAAAAAATACA SEQ.ID.IN:666	-10	-10.4	40.2	0.6	0	-2.1
980	ACAGAGCAAGACTCTGTCTT SEQ.ID.IN:667	-10	-22.9	69.1	-8.4	-4.5	-10.5
1029	GCGGAGGCTGCAGTGAGCCA SEQ.ID.IN:668	-10	-31.1	84.3	-18.5	-2.6	-11.8
1209	CCAGCACTTTGGGAGGCCGA SEQ.ID.IN:669	-10	-29.9	79.4	-18.6	-1.2	-7.7
1260	CCTTTTAAAACTCCAGATGG SEQ.ID.IN:670	-10	-20.8	60.7	-10.8	0	-6.2
1347	ATACAGGAACCCAAGACCCC SEQ.ID.IN:671	-10	-26.7	70.5	-16.7	0.5	-2.9
1358	CAGCTTCCACCATACAGGAA SEQ.ID.IN:672	-10	-25.2	70.4	-14	-1.1	-5.9
1607	AGTTTCCAAACCTTGAAGAT SEQ.ID.IN:673	-10	-20.8	61.3	-10.3	-0.2	-5.3
307	AAAAGGGTTAGGACCCAGAA SEQ.ID.IN:674	-9.9	-21.9	62.5	-7.9	-4.1	-9.2
721	AATGGTTCCCATCAGCCACT SEQ.ID.IN:675	-9.9	-27.6	75.9	-16.1	-1.5	-6
976	AGCAAGACTCTGTCTTGGAA SEQ.ID.IN:676	-9.9	-22.5	67.2	-8.4	-4.2	-12
1010	AGATTGTACCACTTCACTCC SEQ.ID.IN:677	-9.9	-24.3	71.1	-14.4	0	-3.5
1064	GAGGCTGAGGCGGGAGAATC SEQ.ID.IN:678	-9.9	-26.2	73.7	-14.7	-1.6	-4.7
1117	ATACAAAAATTAGCTGGGTA SEQ.ID.IN:679	-9.9	-17.6	54.7	-7.7	0	-4.8
1268	CATGGGAGCCTTTTAAAACT SEQ.ID.IN:680	-9.9	-21.4	62.1	-11.5	0	-6.2
1442	GAAGACTGCAGCAAAGACAT SEQ.ID.IN:681	-9.9	-20.7	61	-10.3	0	-8
1557	GCTGGTCACCCAAAGCTCCC SEQ.ID.IN:682	-9.9	-30.8	81.6	-19.6	-1.2	-8.1
1558	GGCTGGTCACCCAAAGCTCC SEQ.ID.IN:683	-9.9	-30	80.8	-18.1	-2	-8.1
148	AAAGGCCTTCTTCCGCAGCC SEQ.ID.IN:684	-9.8	-29.5	78.4	-18.2	-1.1	-10.6
292	CAGAAAGGAGTAGACGAAGC SEQ.ID.IN:685	-9.8	-19.9	59.4	-10.1	0	-3.5
485	CAGCTGCTGGTCACAGGTGG SEQ.ID.IN:686	-9.8	-28.1	80.9	-15.6	-2.7	-10
559	TCTGGAAGGAACATCAAGTC SEQ.ID.IN:687	-9.8	-20.4	61.9	-10.6	0	-3.2
1068	TCAGGAGGCTGAGGCGGGAG SEQ.ID.IN:688	-9.8	-28.2	78.9	-16.5	-1.9	-7.1
1360	CCCAGCTTCCACCATACAGG SEQ.ID.IN:689	-9.8	-29.3	78.3	-19	-0.2	-4.9
107	CCACCACGTACATCTTGATG SEQ.ID.IN:690	-9.7	-24.4	68	-13.2	-1.4	-7.2
299	TAGGACCCAGAAAGGAGTAG SEQ.ID.IN:691	-9.7	-22.3	64.9	-11.9	-0.4	-4.1
710	TCAGCCACTTCGTGCAGGAA SEQ.ID.IN:692	-9.7	-26.8	74.6	-16	-0.7	-9.8
866	GATTCAGATGATCATTAGGT SEQ.ID.IN:693	-9.7	-20.3	63.1	-9.9	0	-8.7
898	GTCAGTCTGAAAAGTCTGCA SEQ.ID.IN:694	-9.7	-22.3	67.3	-11.9	-0.4	-5.5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1213	CATCCCAGCACTTTGGGAGG SEQ.ID.IN:695	-9.7	-27.8	76.9	-14.7	-3.4	-9.9
1228	GTGATTCATGCCTGTCATCC SEQ.ID.IN:696	-9.7	-26.4	76.4	-16.7	0	-4.4
1436	TGCAGCAAAGACATCCAAAG SEQ.ID.IN:697	-9.7	-20.8	60.3	-11.1	0	-6
1437	CTGCAGCAAAGACATCCAAA SEQ.ID.IN:698	-9.7	-21.7	61.9	-12	0	-7.2
1622	CAAGGGGACATTTGCAGTTT SEQ.ID.IN:699	-9.7	-23.2	67.9	-13.5	0	-5.2
1720	ATGACTAAAAATCACACATC SEQ.ID.IN:700	-9.7	-15.9	51.1	-6.2	0	-3.1
1747	TTTTTTTTTGGCAGACACTT SEQ.ID.IN:701	-9.7	-21.2	64.5	-11.5	0	-4
137	TCCGCAGCCTCACTTGGCCC SEQ.ID.IN:702	-9.6	-33.7	87.3	-22.2	-1.9	-7.1
254	AGATGGTCTCCATGTCGTTC SEQ.ID.IN:703	-9.6	-25.5	75.4	-14.3	-1.6	-6.5
869	CGGGATTCAGATGATCATTA SEQ.ID.IN:704	-9.6	-21.1	62.7	-10.7	-0.5	-8.7
946	ACAGATGGCCAGGCTTGCCT SEQ.ID.IN:705	-9.6	-29.9	81.6	-18.3	-2	-10.5
960	GGAAAAAAAAAAATACAGAT SEQ.ID.IN:706	-9.6	-10	39.4	0	0	-1.2
961	TGGAAAAAAAAAAATACAGA SEQ.ID.IN:707	-9.6	-10	39.5	0	0	-2
1341	GAACCCAAGACCCCAGCCTT SEQ.ID.IN:708	-9.6	-30.4	77.2	-20.8	0	-3.2
1459	CACACCTGAGCCAGAGAGAA SEQ.ID.IN:709	-9.6	-24.9	69.8	-15.3	0.2	-5.7
1707	ACACATCTCAGGTCACGGGT SEQ.ID.IN:710	-9.6	-26.3	75.6	-16.7	0	-3.5
4	CAGCTCAACTGTGGGTGTGA SEQ.ID.IN:711	-9.5	-25.5	74.3	-15.2	-0.6	-4.4
108	GCCACCACGTACATCTTGAT SEQ.ID.IN:712	-9.5	-26.2	72.2	-16.7	0	-5.6
114	ATGATGGCCACCACGTACAT SEQ.ID.IN:713	-9.5	-26	70.7	-15.6	-0.6	-9.1
138	TTCCGCAGCCTCACTTGGCC SEQ.ID.IN:714	-9.5	-31.8	84.4	-20.4	-1.9	-6.8
145	GGCCTTCTTCCGCAGCCTCA SEQ.ID.IN:715	-9.5	-32.9	87.8	-22.2	-1.1	-6.4
166	GGCATCCTCGGGGTTGGCAA SEQ.ID.IN:716	-9.5	-30.1	81.1	-19.1	-1.4	-8.4
839	TCTTAAATAGAGTCTCCCTT SEQ.ID.IN:717	-9.5	-21.9	65.7	-12.4	0	-5.5
944	AGATGGCCAGGCTTGCCTCT SEQ.ID.IN:718	-9.5	-30.3	83.7	-18.8	-2	-11
945	CAGATGGCCAGGCTTGCCTC SEQ.ID.IN:719	-9.5	-30.1	82.8	-18.8	-1.6	-11
1319	TTCCACAGAGAACTGGCAGG SEQ.ID.IN:720	-9.5	-24.6	70.3	-14.1	-0.9	-5.9
1338	CCCAAGACCCCAGCCTTGCT SEQ.ID.IN:721	-9.5	-33	83.2	-22.4	-1	-4.7
1348	CATACAGGAACCCAAGACCC SEQ.ID.IN:722	-9.5	-25.4	68.3	-15.3	-0.3	-3.7
1534	CCTCCACCCACTGCCCTTTG SEQ.ID.IN:723	-9.5	-32.9	84	-23.4	0	-3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1563	TGAGTGGCTGGTCACCCAAA SEQ.ID.IN:724	-9.5	-26.7	73.9	-15.6	-1.5	-7.9
1626	CCATCAAGGGGACATTTGCA SEQ.ID.IN:725	-9.5	-24.9	69.9	-15.4	0	-4.8
71	AGAGCAGGAAGGCCGGGAGG SEQ.ID.IN:726	-9.4	-28.2	76.8	-17.6	-1.1	-7.7
96	ATCTTGATGACCAGCAGCGT SEQ.ID.IN:727	-9.4	-25.8	72.8	-16.4	5.1	-5.4
194	TGCAATACTGGGGGCCTCCG SEQ.ID.IN:728	-9.4	-29.3	77.3	-18.1	-1.1	-11.6
372	CCCAGGTAGGCCACGGTGTG SEQ.ID.IN:729	-9.4	-31.1	82.8	-20.4	-1.2	-7.7
718	GGTTCCCATCAGCCACTTCG SEQ.ID.IN:730	-9.4	-29.6	80.4	-20.2	0	-3.2
1108	TTAGCTGGGTATGGTGATAC SEQ.ID.IN:731	-9.4	-22.7	68.5	-12.4	-0.7	-8.8
1418	AGCCAACGGCAAGGGAAGCG SEQ.ID.IN:732	-9.4	-26.7	70	-14.8	-2.5	-8.2
1650	CACACACACACACACACGGA SEQ.ID.IN:733	-9.4	-23.8	65.9	-14.4	0	-3.5
1732	CACTTCCATTTAATGACTAA SEQ.ID.IN:734	-9.4	-18.9	57.5	-9.5	0	-3.9
1733	ACACTTCCATTTAATGACTA SEQ.ID.IN:735	-9.4	-19.8	60	-10.4	0	-3.9
68	GCAGGAAGGCCGGGAGGGCC SEQ.ID.IN:736	-9.3	-32.6	84.8	-19.3	-4	-11.4
129	CTCACTTGGCCCGTGATGAT SEQ.ID.IN:737	-9.3	-27.4	74.7	-16.6	-1	-10.5
208	GTCGGGGTCGCTCCTGCAAT SEQ.ID.IN:738	-9.3	-30.2	81.4	-19.5	-1.3	-6.1
260	AGGGGTAGATGGTCTCCATG SEQ.ID.IN:739	-9.3	-25.9	75.9	-15	-1.6	-6.5
369	AGGTAGGCCACGGTGTGTGC SEQ.ID.IN:740	-9.3	-29.4	82.7	-18.6	-1.4	-7.7
430	GGCGCAGGGGAGCTGGGCCA SEQ.ID.IN:741	-9.3	-34.1	89.4	-18.1	-6.7	-13.4
1110	AATTAGCTGGGTATGGTGAT SEQ.ID.IN:742	-9.3	-22.1	66.2	-12.8	0	-4.8
42	CTCATCACCAGGCTGTGGGC SEQ.ID.IN:743	-9.2	-29.3	82.5	-18.5	-1.5	-5.9
130	CCTCACTTGGCCCGTGATGA SEQ.ID.IN:744	-9.2	-29.4	78.1	-18.7	-1	-10.5
313	GGCGACAAAAGGGTTAGGAC SEQ.ID.IN:745	-9.2	-22.6	64.4	-13.4	0	-4
533	TATAGCCACGGCGGCTCTTG SEQ.ID.IN:746	-9.2	-28	75.6	-15.7	-3.1	-10
536	AGGTATAGCCACGGCGGCTC SEQ.ID.IN:747	-9.2	-29.4	79.7	-17.1	-3.1	-10.9
809	ACTGTTAGGGAGGGAGAGGG SEQ.ID.IN:748	-9.2	-25.1	74	-15.9	0	-2.4
943	GATGGCCAGGCTTGCCTCTA SEQ.ID.IN:749	-9.2	-30	82.8	-18.8	-2	-11
955	AAAAAAAATACAGATGGCCA SEQ.ID.IN:750	-9.2	-16	49.9	-6.1	0	-8.8
975	GCAAGACTCTGTCTTGGAAA SEQ.ID.IN:751	-9.2	-21.8	64.7	-8.4	-4.2	-12
988	CTTGGGCAACAGAGCAAGAC SEQ.ID.IN:752	-9.2	-23.3	67.1	-13.2	-0.8	-5.2

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1069	CTCAGGAGGCTGAGGCGGGA SEQ.ID.IN:753	-9.2	-29.1	80.5	-16.5	-3.4	-11.1
1106	AGCTGGGTATGGTGATACGC SEQ.ID.IN:754	-9.2	-25.5	73.2	-16.3	4.4	-6.9
1109	ATTAGCTGGGTATGGTGATA SEQ.ID.IN:755	-9.2	-22.5	67.9	-13.3	0	-4.8
1335	AAGACCCCAGCCTTGCTTCC SEQ.ID.IN:756	-9.2	-30.8	81.2	-20.9	-0.5	-4.2
1343	AGGAACCCAAGACCCCAGCC SEQ.ID.IN:757	-9.2	-30.6	77.7	-20.8	-0.3	-3.7
1376	CCCTGTCCTTGGCTCACCCA SEQ.ID.IN:758	-9.2	-33.4	87.5	-23.3	-0.7	-3.7
1457	CACCTGAGCCAGAGAGAAGA SEQ.ID.IN:759	-9.2	-24.6	69.6	-14.8	-0.3	-6.2
1535	TCCTCCACCCACTGCCCTTT SEQ.ID.IN:760	-9.2	-33.3	85.9	-24.1	0	-3
1605	TTTCCAAACCTTGAAGATAC SEQ.ID.IN:761	-9.2	-19.5	58.2	-10.3	0	-2.9
3	AGCTCAACTGTGGGTGTGAT SEQ.ID.IN:762	-9.1	-24.8	73.1	-15.2	-0.1	-4.3
97	CATCTTGATGACCAGCAGCG SEQ.ID.IN:763	-9.1	-25.3	70.7	-15.2	-0.9	-7.2
308	CAAAAGGGTTAGGACCCAGA SEQ.ID.IN:764	-9.1	-23.3	65.6	-10.9	-3.3	-8.4
338	CGAGGAAGACCAGGAAGTGC SEQ.ID.IN:765	-9.1	-24.1	67.6	-13.6	-1.3	-5
383	CCCGCAGCTTCCCCAGGTAG SEQ.ID.IN:766	-9.1	-33.3	85.9	-24.2	0	-4.4
790	GAGTGATGTTTTTGATGCTC SEQ.ID.IN:767	-9.1	-21.7	67	-12.6	0	-3.6
962	TTGGAAAAAAAAAAATACAG SEQ.ID.IN:768	-9.1	-9.5	38.7	0	0	-2.3
1284	CCATCACAGGGACTCACATG SEQ.ID.IN:769	-9.1	-24.8	70.5	-15.1	-0.3	-5.1
1345	ACAGGAACCCAAGACCCCAG SEQ.ID.IN:770	-9.1	-27.7	72.3	-18	-0.3	-3.7
1349	CCATACAGGAACCCAAGACC SEQ.ID.IN:771	-9.1	-25.4	68.3	-15.7	-0.3	-3.7
1420	AAAGCCAACGGCAAGGGAAG SEQ.ID.IN:772	-9.1	-22.7	62.4	-11.1	-2.5	-7.6
1717	ACTAAAAATCACACATCTCA SEQ.ID.IN:773	-9.1	-17.3	54.1	-8.2	0	-1.1
172	TCTCAGGGCATCCTCGGGGT SEQ.ID.IN:774	-9	-30.6	85.3	-20.6	-0.9	-7
182	GGCCTCCGTGTCTCAGGGCA SEQ.ID.IN:775	-9	-32.8	89.6	-21.6	-2.2	-9.2
190	ATACTGGGGGCCTCCGTGTC SEQ.ID.IN:776	-9	-30.3	83.2	-19.7	-1.1	-11.2
291	AGAAAGGAGTAGACGAAGCC SEQ.ID.IN:777	-9	-21.2	61.8	-12.2	0	-3.5
314	AGGCGACAAAAGGGTTAGGA SEQ.ID.IN:778	-9	-22.4	64.1	-13.4	0	-4
319	CATCCAGGCGACAAAAGGGT SEQ.ID.IN:779	-9	-24.6	67.5	-15.6	0	-4
367	GTAGGCCACGGTGTGTGCCA SEQ.ID.IN:780	-9	-30.9	84.2	-17.6	-4.3	-11.9
958	AAAAAAAAAAATACAGATGG SEQ.ID.IN:781	-9	-9.4	38.5	0	0	-2.4

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1009	GATTGTACCACTTCACTCCA SEQ.ID.IN:782	-9	-25	71.9	-16	0	-4.2
1033	GGAGGCGGAGGCTGCAGTGA SEQ.ID.IN:783	-9	-29.6	82	-18.6	-2	-8.9
1332	ACCCCAGCCTTGCTTCCACA SEQ.ID.IN:784	-9	-32.5	84.6	-22.9	-0.3	-4
1612	TTTGCAGTTTCCAAACCTTG SEQ.ID.IN:785	-9	-23	66.3	-13.5	-0.2	-5.3
33	AGGCTGTGGGCAGGCATCTC SEQ.ID.IN:786	-8.9	-29.4	85	-18.9	-1.5	-5.5
528	CCACGGCGGCTCTTGGCCCA SEQ.ID.IN:787	-8.9	-34.5	86.1	-23.3	-2.3	-7.7
538	CCAGGTATAGCCACGGCGGC SEQ.ID.IN:788	-8.9	-30.8	80.4	-19.8	-2.1	-8.2
840	ATCTTAAATAGAGTCTCCCT SEQ.ID.IN:789	-8.9	-21.8	65.3	-12.4	-0.1	-5.5
1031	AGGCGGAGGCTGCAGTGAGC SEQ.ID.IN:790	-8.9	-29.6	82.9	-17.9	-2.8	-8.9
1111	AAATTAGCTGGGTATGGTGA SEQ.ID.IN:791	-8.9	-21.4	64	-12.5	0	-4.5
1275	GGACTCACATGGGAGCCTTT SEQ.ID.IN:792	-8.9	-26.8	75.9	-16.6	-1.2	-9.5
1282	ATCACAGGGACTCACATGGG SEQ.ID.IN:793	-8.9	-24.5	70.9	-15.1	-0.1	-5.4
105	ACCACGTACATCTTGATGAC SEQ.ID.IN:794	-8.8	-22.5	65.2	-11.9	-1.8	-9.6
477	GGTCACAGGTGGCGGGCCGC SEQ.ID.IN:795	-8.8	-33.4	87.9	-22.8	-1.8	-9.9
701	TCGTGCAGGAATCCAAGGGG SEQ.ID.IN:796	-8.8	-26	71.7	-16.6	-0.3	-7.8
1005	GTACCACTTCACTCCAGCTT SEQ.ID.IN:797	-8.8	-27.1	77.5	-18.3	0	-4.5
1271	TCACATGGGAGCCTTTTAAA SEQ.ID.IN:798	-8.8	-22.3	64.7	-13.5	0	-5.9
1352	CCACCATACAGGAACCCAAG SEQ.ID.IN:799	-8.8	-25.5	68.2	-15.9	-0.6	-4
1604	TTCCAAACCTTGAAGATACT SEQ.ID.IN:800	-8.8	-20.3	59.7	-11.5	0	-2.8
1748	TTTTTTTTTTGGCAGACACT SEQ.ID.IN:801	-8.8	-21.2	64.5	-12.4	0	-4
171	CTCAGGGCATCCTCGGGGTT SEQ.ID.IN:802	-8.7	-30.3	83.7	-20.6	-0.9	-7
249	GTCTCCATGTCGTTCCGGTG SEQ.ID.IN:803	-8.7	-28.9	80.7	-20.2	0	-6.6
259	GGGGTAGATGGTCTCCATGT SEQ.ID.IN:804	-8.7	-27.1	79.3	-16.8	-1.6	-6.5
305	AAGGGTTAGGACCCAGAAAG SEQ.ID.IN:805	-8.7	-22.6	64.7	-9.8	-4.1	-9.2
576	CTCAGGGCCCACCACAATCT SEQ.ID.IN:806	-8.7	-29.3	78.4	-18.9	-1.2	-11.3
754	GGATTTTCTATCAATCTTCA SEQ.ID.IN:807	-8.7	-20	62.3	-10.3	-0.9	-4.9
981	AACAGAGCAAGACTCTGTCT SEQ.ID.IN:808	-8.7	-22.1	66.3	-8.4	-5	-11.3
983	GCAACAGAGCAAGACTCTGT SEQ.ID.IN:809	-8.7	-23.3	68.3	-9.8	-4.8	-11.4
1001	CACTTCACTCCAGCTTGGGC SEQ.ID.IN:810	-8.7	-28.2	79.9	-18.5	-0.9	-6.4

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1006	TGTACCACTTCACTCCAGCT SEQ.ID.IN:811	-8.7	-27	76.9	-18.3	0	-4.3
1037	CCCGGGAGGCGGAGGCTGCA SEQ.ID.IN:812	-8.7	-33.8	85.5	-22.6	-2.4	-12.4
1435	GCAGCAAAGACATCCAAAGC SEQ.ID.IN:813	-8.7	-22.6	64.2	-13.9	0	-4.7
1478	CCTGTGGGCCCCTCCCACCC SEQ.ID.IN:814	-8.7	-38.5	94.1	-25	-4.8	-10.7
1713	AAAATCACACATCTCAGGTC SEQ.ID.IN:815	-8.7	-20	61	-11.3	0	-2.5
327	AGGAAGTGCATCCAGGCGAC SEQ.ID.IN:816	-8.6	-26.5	73.8	-16.3	-1.5	-8.7
482	CTGCTGGTCACAGGTGGCGG SEQ.ID.IN:817	-8.6	-29.4	81.6	-19.2	-1.5	-7.3
756	AAGGATTTTCTATCAATCTT SEQ.ID.IN:818	-8.6	-18.2	57.7	-8.6	-0.9	-4.4
870	CCGGGATTCAGATGATCATT SEQ.ID.IN:819	-8.6	-23.4	66.9	-14	-0.5	-8.7
1536	GTCCTCCACCCACTGCCCTT SEQ.ID.IN:820	-8.6	-34.4	89	-25.8	0	-3
1721	AATGACTAAAAATCACACAT SEQ.ID.IN:821	-8.6	-14.8	48.5	-6.2	0	-3.2
136	CCGCAGCCTCACTTGGCCCG SEQ.ID.IN:822	-8.5	-34.1	84.8	-24	-1.6	-7.1
209	CGTCGGGGTCGCTCCTGCAA SEQ.ID.IN:823	-8.5	-31	80.9	-21.1	-1.3	-6.1
218	AGCGTTCCACGTCGGGGTCG SEQ.ID.IN:824	-8.5	-30.4	80	-18.7	-3.2	-8.7
791	GGAGTGATGTTTTTGATGCT SEQ.ID.IN:825	-8.5	-22.5	68.1	-14	0	-3.6
940	GGCCAGGCTTGCCTCTAGAT SEQ.ID.IN:826	-8.5	-30	83.4	-19.9	-1.6	-9.4
972	AGACTCTGTCTTGGAAAAAA SEQ.ID.IN:827	-8.5	-17.9	55.6	-8.4	-0.9	-5.4
1032	GAGGCGGAGGCTGCAGTGAG SEQ.ID.IN:828	-8.5	-28.4	79.7	-17.9	-2	-8.9
1063	AGGCTGAGGCGGGAGAATCG SEQ.ID.IN:829	-8.5	-26.4	72.4	-15.5	-2.4	-5.7
1312	GAGAACTGGCAGGGGTCCCC SEQ.ID.IN:830	-8.5	-30.5	82.4	-20.9	-1	-8.2
318	ATCCAGGCGACAAAAGGGTT SEQ.ID.IN:831	-8.4	-24	66.7	-15.6	0	-4
370	CAGGTAGGCCACGGTGTGTG SEQ.ID.IN:832	-8.4	-28.3	79.2	-18.6	-1.2	-7.7
531	TAGCCACGGCGGCTCTTGGC SEQ.ID.IN:833	-8.4	-31.3	82.8	-19.8	-3.1	-12.1
727	TCTTGAAATGGTTCCCATCA SEQ.ID.IN:834	-8.4	-23.3	67.1	-13.3	-1.5	-5.9
902	TGGGGTCAGTCTGAAAAGTC SEQ.ID.IN:835	-8.4	-22.5	67.8	-13.4	-0.4	-6.1
959	GAAAAAAAAAAATACAGATG SEQ.ID.IN:836	-8.4	-8.8	37.5	0	0	-2.1
1003	ACCACTTCACTCCAGCTTGG SEQ.ID.IN:837	-8.4	-27.4	77	-18.3	-0.5	-5.8
1120	AAAATACAAAAATTAGCTGG SEQ.ID.IN:838	-8.4	-13.4	45.7	-5	0	-4.8
1461	CCCACACCTGAGCCAGAGAG SEQ.ID.IN:839	-8.4	-29	77.7	-20	-0.3	-6.2

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1737	GCAGACACTTCCATTTAATG SEQ.ID.IN:840	-8.4	-21.5	63.5	-13.1	0	-3.4
149	CAAAGGCCTTCTTCCGCAGC SEQ.ID.IN:841	-8.3	-28.2	76.1	-18.6	-0.3	-10.6
184	GGGGCCTCCGTGTCTCAGGG SEQ.ID.IN:842	-8.3	-32.7	89.4	-22.4	-1.1	-12
220	GCAGCGTTCCACGTCGGGGT SEQ.ID.IN:843	-8.3	-31.7	83.9	-22.1	-1.2	-8.4
895	AGTCTGAAAAGTCTGCATTC SEQ.ID.IN:844	-8.3	-20.5	63.1	-11.5	-0.4	-5.7
954	AAAAAAATACAGATGGCCAG SEQ.ID.IN:845	-8.3	-16.7	51.5	-7.7	0	-9.1
971	GACTCTGTCTTGGAAAAAAA SEQ.ID.IN:846	-8.3	-17.2	53.7	-8.4	-0.1	-4
1114	CAAAAATTAGCTGGGTATGG SEQ.ID.IN:847	-8.3	-18.9	57.1	-10.6	0	-4.8
1226	GATTCATGCCTGTCATCCCA SEQ.ID.IN:848	-8.3	-27.9	77.8	-19.6	0	-4.4
1351	CACCATACAGGAACCCAAGA SEQ.ID.IN:849	-8.3	-24.1	66	-15	-0.6	-4
1375	CCTGTCCTTGGCTCACCCAG SEQ.ID.IN:850	-8.3	-31.4	84.6	-22.1	-0.9	-4
1458	ACACCTGAGCCAGAGAGAAG SEQ.ID.IN:851	-8.3	-24.2	68.9	-15.3	-0.3	-6.2
1722	TAATGACTAAAAATCACACA SEQ.ID.IN:852	-8.3	-14.5	48	-6.2	0	-3.1
1734	GACACTTCCATTTAATGACT SEQ.ID.IN:853	-8.3	-20.7	61.8	-12.4	0	-3.9
31	GCTGTGGGCAGGCATCTCTG SEQ.ID.IN:854	-8.2	-29.1	83.6	-19.4	-1.4	-5.8
160	CTCGGGGTTGGCAAAGGCCT SEQ.ID.IN:855	-8.2	-29.2	78.2	-18	-3	-8.4
165	GCATCCTCGGGGTTGGCAAA SEQ.ID.IN:856	-8.2	-28.2	76.2	-19.1	-0.8	-8
825	TCCCTTCTCTCTTTTCACTG SEQ.ID.IN:857	-8.2	-25.8	76.2	-17.6	0	-1.5
903	CTGGGGTCAGTCTGAAAAGT SEQ.ID.IN:858	-8.2	-23	68.2	-12.1	-2.7	-7.2
915	GGGCCAGAATTTCTGGGGTC SEQ.ID.IN:859	-8.2	-27.5	78.2	-15.7	-3.6	-13.5
1023	GCTGCAGTGAGCCAGATTGT SEQ.ID.IN:860	-8.2	-27.4	78.8	-18.3	-0.8	-8.7
1036	CCGGGAGGCGGAGGCTGCAG SEQ.ID.IN:861	-8.2	-31.8	82.7	-21.4	-2	-12
1067	CAGGAGGCTGAGGCGGGAGA SEQ.ID.IN:862	-8.2	-28.4	78.5	-18.6	-1.6	-4.8
1113	AAAAATTAGCTGGGTATGGT SEQ.ID.IN:863	-8.2	-19.4	58.7	-11.2	0	-4.8
1362	CACCCAGCTTCCACCATACA SEQ.ID.IN:864	-8.2	-29	77.2	-20.8	0	-4.3
1412	CGGCAAGGGAAGCGTCAGCG SEQ.ID.IN:865	-8.2	-27.6	72.7	-17.7	-1.7	-6.6
1727	CCATTTAATGACTAAAAATC SEQ.ID.IN:866	-8.2	-14.9	48.8	-6.2	-0.1	-3.9
1728	TCCATTTAATGACTAAAAAT SEQ.ID.IN:867	-8.2	-14.9	48.8	-6.2	-0.1	-3.9
20	GCATCTCTGGCCAGCGCAGC SEQ.ID.IN:868	-8.1	-31.7	86.4	-21.6	-1.6	-11.9

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
317	TCCAGGCGACAAAAGGGTTA SEQ.ID.IN:869	-8.1	-23.7	66.2	-15.6	0	-3.6
830	GAGTCTCCCTTCTCTCTTTT SEQ.ID.IN:870	-8.1	-26.7	80.2	-18.1	-0.1	-3.9
941	TGGCCAGGCTTGCCTCTAGA SEQ.ID.IN:871	-8.1	-30	83.2	-19.9	-2	-10.2
964	TCTTGGAAAAAAAAAAATAC SEQ.ID.IN:872	-8.1	-10.1	39.8	-2	0	-2.1
1119	AAATACAAAAATTAGCTGGG SEQ.ID.IN:873	-8.1	-15.3	49.4	-7.2	0	-4.8
1121	AAAAATACAAAAATTAGCTG SEQ.ID.IN:874	-8.1	-11.5	42.2	-3.4	0	-4.8
115	GATGATGGCCACCACGTACA SEQ.ID.IN:875	-7.9	-26.6	72	-18	-0.2	-8.6
128	TCACTTGGCCCGTGATGATG SEQ.ID.IN:876	-7.9	-26.5	72.7	-17.3	-0.8	-10.2
315	CAGGCGACAAAAGGGTTAGG SEQ.ID.IN:877	-7.9	-22.5	64	-14.6	0	-4
503	TGGTGGCCAAGGAGGCATCA SEQ.ID.IN:878	-7.9	-28	77.8	-17.5	-2.6	-9.4
586	GAAACCAGGACTCAGGGCCC SEQ.ID.IN:879	-7.9	-28.3	75.8	-19.4	0	-10
808	CTGTTAGGGAGGGAGAGGGA SEQ.ID.IN:880	-7.9	-25.5	74.8	-17.6	0	-1.5
1007	TTGTACCACTTCACTCCAGC SEQ.ID.IN:881	-7.9	-26.2	75.3	-18.3	0	-4.2
1070	ACTCAGGAGGCTGAGGCGGG SEQ.ID.IN:882	-7.9	-28.7	79.8	-16.5	-4.3	-12.2
1336	CAAGACCCCAGCCTTGCTTC SEQ.ID.IN:883	-7.9	-29.5	78.9	-20.9	-0.5	-4.4
1468	CCTCCCACCCACACCTGAGC SEQ.ID.IN:884	-7.9	-33.3	84.7	-25.4	0	-3.3
189	TACTGGGGGCCTCCGTGTCT SEQ.ID.IN:885	-7.8	-31.2	85.2	-21.5	-1.1	-11.8
204	GGGTCGCTCCTGCAATACTG SEQ.ID.IN:886	-7.8	-27.4	75.8	-18.7	-0.8	-6.4
207	TCGGGGTCGCTCCTGCAATA SEQ.ID.IN:887	-7.8	-28.7	77.4	-19.5	-1.3	-6.1
499	GGCCAAGGAGGCATCAGCTG SEQ.ID.IN:888	-7.8	-28.3	78.5	-17.1	-3.4	-13.8
1122	TAAAAATACAAAAATTAGCT SEQ.ID.IN:889	-7.8	-11.2	41.7	-3.4	0	-4.4
1273	ACTCACATGGGAGCCTTTTA SEQ.ID.IN:890	-7.8	-24.8	71.7	-16.3	-0.4	-8.1
1333	GACCCCAGCCTTGCTTCCAC SEQ.ID.IN:891	-7.8	-32.4	84.9	-23.9	-0.5	-4.2
1350	ACCATACAGGAACCCAAGAC SEQ.ID.IN:892	-7.8	-23.6	65.5	-15	-0.6	-4
1462	ACCCACACCTGAGCCAGAGA SEQ.ID.IN:893	-7.8	-29.2	77.9	-20.8	-0.3	-6.2
1470	CCCCTCCCACCCACACCTGA SEQ.ID.IN:894	-7.8	-35.5	86.4	-27.7	0	-2
5	GCAGCTCAACTGTGGGTGTG SEQ.ID.IN:895	-7.7	-26.7	77.4	-17.6	-1.3	-6.5
98	ACATCTTGATGACCAGCAGC SEQ.ID.IN:896	-7.7	-24.7	71.3	-15.2	-1.8	-7.4
476	GTCACAGGTGGCGGGCCGCT SEQ.ID.IN:897	-7.7	-33.1	87.3	-22.8	-2.6	-10.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
843	GGAATCTTAAATAGAGTCTC SEQ.ID.IN:898	-7.7	-18	57.4	-8.2	-2.1	-5.5
973	AAGACTCTGTCTTGGAAAAA SEQ.ID.IN:899	-7.7	-17.9	55.6	-8.4	-1.8	-7.3
1021	TGCAGTGAGCCAGATTGTAC SEQ.ID.IN:900	-7.7	-24.6	72.3	-16	-0.8	-5
1053	GGGAGAATCGCTTGAACCCG SEQ.ID.IN:901	-7.7	-25.8	68.7	-17	-1	-5.5
1259	CTTTTAAAACTCCAGATGGT SEQ.ID.IN:902	-7.7	-20	60	-12.3	0	-6.2
1269	ACATGGGAGCCTTTTAAAAC SEQ.ID.IN:903	-7.7	-20.7	60.8	-13	0	-6.2
1627	CCCATCAAGGGGACATTTGC SEQ.ID.IN:904	-7.7	-26.2	72.3	-16.9	-1.5	-5.6
1723	TTAATGACTAAAAATCACAC SEQ.ID.IN:905	-7.7	-13.9	47	-6.2	0	-3.1
95	TCTTGATGACCAGCAGCGTG SEQ.ID.IN:906	-7.6	-25.8	72.7	-18.2	4.4	-5.4
192	CAATACTGGGGGCCTCCGTG SEQ.ID.IN:907	-7.6	-28.7	76.5	-19.2	-1.1	-11.8
206	CGGGGTCGCTCCTGCAATAC SEQ.ID.IN:908	-7.6	-28.5	76.3	-19.5	-1.3	-6.4
214	TTCCACGTCGGGGTCGCTCC SEQ.ID.IN:909	-7.6	-31.7	83.6	-23.4	-0.4	-6.8
522	CGGCTCTTGGCCCATGGTCT SEQ.ID.IN:910	-7.6	-31.5	84.7	-21.6	-2.3	-9.3
530	AGCCACGGCGGCTCTTGGCC SEQ.ID.IN:911	-7.6	-33.6	86.6	-23.1	-2.9	-12.5
539	CCCAGGTATAGCCACGGCGG SEQ.ID.IN:912	-7.6	-31	79.6	-22.2	-1.1	-8.2
1004	TACCACTTCACTCCAGCTTG SEQ.ID.IN:913	-7.6	-25.9	73.8	-18.3	0	-4.5
1286	GGCCATCACAGGGACTCACA SEQ.ID.IN:914	-7.6	-27.8	77.6	-19.6	-0.3	-7.4
1438	ACTGCAGCAAAGACATCCAA SEQ.ID.IN:915	-7.6	-22.6	64.3	-14.3	0	-8.9
1556	CTGGTCACCCAAAGCTCCCG SEQ.ID.IN:916	-7.6	-29.8	77.2	-21.2	-0.9	-8.1
1724	TTTAATGACTAAAAATCACA SEQ.ID.IN:917	-7.6	-13.8	46.8	-6.2	0	-3.1
69	AGCAGGAAGGCCGGGAGGGC SEQ.ID.IN:918	-7.5	-30.6	81.9	-20.9	-2.2	-8.5
163	ATCCTCGGGGTTGGCAAAGG SEQ.ID.IN:919	-7.5	-26.9	73.8	-18.9	-0.2	-7
217	GCGTTCCACGTCGGGGTCGC SEQ.ID.IN:920	-7.5	-32.2	83.8	-21.5	-3.2	-10.2
532	ATAGCCACGGCGGCTCTTGG SEQ.ID.IN:921	-7.5	-29.5	78.6	-18.9	-3.1	-10
970	ACTCTGTCTTGGAAAAAAAA SEQ.ID.IN:922	-7.5	-15.9	50.9	-8.4	0	-2.6
1361	ACCCAGCTTCCACCATACAG SEQ.ID.IN:923	-7.5	-28.3	76.5	-20.8	0	-4.5
1751	TTTTTTTTTTTTTGGCAGAC SEQ.ID.IN:924	-7.5	-19.7	61.7	-12.2	0	-4
293	CCAGAAAGGAGTAGACGAAG SEQ.ID.IN:925	-7.4	-20.1	59.1	-12.7	0	-3.5
304	AGGGTTAGGACCCAGAAAGG SEQ.ID.IN:926	-7.4	-24.5	69.3	-13	-4.1	-9.2

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
939	GCCAGGCTTGCCTCTAGATT SEQ.ID.IN:927	-7.4	-28.9	81.1	-19.9	-1.6	-8.9
942	ATGGCCAGGCTTGCCTCTAG SEQ.ID.IN:928	-7.4	-29.4	81.8	-20	-2	-11
974	CAAGACTCTGTCTTGGAAAA SEQ.ID.IN:929	-7.4	-19.3	58.6	-8.4	-3.5	-10.7
1027	GGAGGCTGCAGTGAGCCAGA SEQ.ID.IN:930	-7.4	-29.1	82.2	-18.3	-3.4	-12.6
1102	GGGTATGGTGATACGCGCCT SEQ.ID.IN:931	-7.4	-28.3	76.4	-19.2	-1.7	-9.8
1103	TGGGTATGGTGATACGCGCC SEQ.ID.IN:932	-7.4	-27.4	74.4	-18.2	-1.8	-9.8
1212	ATCCCAGCACTTTGGGAGGC SEQ.ID.IN:933	-7.4	-28.9	80.2	-18.1	-3.4	-9.9
1285	GCCATCACAGGGACTCACAT SEQ.ID.IN:934	-7.4	-26.6	74.9	-18.6	-0.3	-4
1298	GTCCCCTGGCCTGGCCATCA SEQ.ID.IN:935	-7.4	-35.2	91.4	-24.5	-2.5	-14.5
1371	TCCTTGGCTCACCCAGCTTC SEQ.ID.IN:936	-7.4	-30.5	84.5	-21.3	-1.8	-5.2
1415	CAACGGCAAGGGAAGCGTCA SEQ.ID.IN:937	-7.4	-25.2	68.1	-16.8	-0.9	-6
1752	TTTTTTTTTTTTTTGGCAGA SEQ.ID.IN:938	-7.4	-19.6	61.5	-12.2	0	-4
1	CTCAACTGTGGGTGTGATCA SEQ.ID.IN:939	-7.3	-24.1	71.2	-16.3	-0.1	-6.5
99	TACATCTTGATGACCAGCAG SEQ.ID.IN:940	-7.3	-22.6	66.4	-13.5	-1.8	-7.4
303	GGGTTAGGACCCAGAAAGGA SEQ.ID.IN:941	-7.3	-25.1	70.3	-14.5	-3.3	-8.5
871	CCCGGGATTCAGATGATCAT SEQ.ID.IN:942	-7.3	-25.3	70.1	-17.3	0.2	-9.2
1554	GGTCACCCAAAGCTCCCGGT SEQ.ID.IN:943	-7.3	-31.3	81.1	-23.5	-0.1	-6.4
22	AGGCATCTCTGGCCAGCGCA SEQ.ID.IN:944	-7.2	-31.1	84.5	-21.1	-2.6	-12.9
175	GTGTCTCAGGGCATCCTCGG SEQ.ID.IN:945	-7.2	-29.4	83.4	-21.2	-0.9	-6.5
523	GCGGCTCTTGGCCCATGGTC SEQ.ID.IN:946	-7.2	-32.4	87.2	-22.9	-2.3	-9.3
645	CACGGGCACACACACAGGCC SEQ.ID.IN:947	-7.2	-29.2	77.2	-20.6	-1.3	-6.4
989	GCTTGGGCAACAGAGCAAGA SEQ.ID.IN:948	-7.2	-24.9	70.6	-16	-1.7	-7.2
1000	ACTTCACTCCAGCTTGGGCA SEQ.ID.IN:949	-7.2	-28.2	79.9	-19.4	-1.6	-6.4
1002	CCACTTCACTCCAGCTTGGG SEQ.ID.IN:950	-7.2	-28.4	79	-20.2	-0.9	-6.4
1344	CAGGAACCCAAGACCCCAGC SEQ.ID.IN:951	-7.2	-29.3	75.6	-21.5	-0.3	-3.7
1484	GAGCTTCCTGTGGGCCCCTC SEQ.ID.IN:952	-7.2	-33.4	90.4	-25	-0.1	-10.3
210	ACGTCGGGGTCGCTCCTGCA SEQ.ID.IN:953	-7.1	-31.9	84	-23.4	-1.3	-7.9
321	TGCATCCAGGCGACAAAAGG SEQ.ID.IN:954	-7.1	-24	65.9	-16	-0.7	-4.7
894	GTCTGAAAAGTCTGCATTCT SEQ.ID.IN:955	-7.1	-21.4	64.9	-13.6	-0.4	-5.7

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1035	CGGGAGGCGGAGGCTGCAGT SEQ.ID.IN:956	-7.1	-31	82.9	-21.9	-2	-8.9
1313	AGAGAACTGGCAGGGGTCCC SEQ.ID.IN:957	-7.1	-28.5	79.3	-20.9	-0.2	-6.4
1479	TCCTGTGGGCCCCTCCCACC SEQ.ID.IN:958	-7.1	-36.9	93.1	-25	-4.8	-10.7
1649	ACACACACACACACACGGAT SEQ.ID.IN:959	-7.1	-23.1	64.8	-16	0	-3.5
17	TCTCTGGCCAGCGCAGCTCA SEQ.ID.IN:960	-7	-31.2	85.9	-21.6	-2.5	-12.4
23	CAGGCATCTCTGGCCAGCGC SEQ.ID.IN:961	-7	-31.1	84.5	-21.5	-2.6	-11.9
521	GGCTCTTGGCCCATGGTCTG SEQ.ID.IN:962	-7	-30.7	85.1	-21.9	-1.8	-9.3
1038	ACCCGGGAGGCGGAGGCTGC SEQ.ID.IN:963	-7	-33.3	85.2	-23.7	-2.4	-12.9
1377	GCCCTGTCCTTGGCTCACCC SEQ.ID.IN:964	-7	-34.5	90.9	-26.1	-1.3	-5.4
1469	CCCTCCCACCCACACCTGAG SEQ.ID.IN:965	-7	-33.5	83.8	-26.5	0	-3.2
1475	GTGGGCCCCTCCCACCCACA SEQ.ID.IN:966	-7	-37.2	91.9	-25.9	-4.3	-11.1
1678	AACACACACACACACACACA SEQ.ID.IN:967	-7	-21.4	61.7	-14.4	0	0
1749	TTTTTTTTTTTGGCAGACAC SEQ.ID.IN:968	-7	-20.4	62.9	-13.4	0	-4
45	CTGCTCATCACCAGGCTGTG SEQ.ID.IN:969	-6.9	-27.8	78.9	-20.4	-0.2	-4.3
161	CCTCGGGGTTGGCAAAGGCC SEQ.ID.IN:970	-6.9	-30.3	79.6	-21.2	-2.2	-10.2
173	GTCTCAGGGCATCCTCGGGG SEQ.ID.IN:971	-6.9	-30.6	85.3	-22.8	-0.7	-6.4
504	CTGGTGGCCAAGGAGGCATC SEQ.ID.IN:972	-6.9	-28.2	78.7	-17.9	-3.4	-9
952	AAAAATACAGATGGCCAGGC SEQ.ID.IN:973	-6.9	-21.1	60.7	-13.5	0	-9.1
1281	TCACAGGGACTCACATGGGA SEQ.ID.IN:974	-6.9	-25.1	72.3	-17.6	-0.3	-6
1726	CATTTAATGACTAAAAATCA SEQ.ID.IN:975	-6.9	-13.6	46.4	-6.2	-0.1	-3.1
109	GGCCACCACGTACATCTTGA SEQ.ID.IN:976	-6.8	-27.4	74.7	-20.6	0	-7
176	CGTGTCTCAGGGCATCCTCG SEQ.ID.IN:977	-6.8	-29	80.2	-21.2	-0.9	-5
181	GCCTCCGTGTCTCAGGGCAT SEQ.ID.IN:978	-6.8	-31.6	86.9	-23.3	-1.4	-7.7
195	CTGCAATACTGGGGGCCTCC SEQ.ID.IN:979	-6.8	-29.4	79.5	-21.5	0	-10.2
700	CGTGCAGGAATCCAAGGGGC SEQ.ID.IN:980	-6.8	-27.4	74.2	-20	-0.3	-6.9
953	AAAAAATACAGATGGCCAGG SEQ.ID.IN:981	-6.8	-18.6	55.4	-11.1	0	-9.1
965	GTCTTGGAAAAAAAAAAATA SEQ.ID.IN:982	-6.8	-11.1	41.5	-4.3	0	-2.6
1185	GGTGGATCACTTGAGGCCAG SEQ.ID.IN:983	-6.8	-26.8	76.5	-18.3	-1.7	-9.2
19	CATCTCTGGCCAGCGCAGCT SEQ.ID.IN:984	-6.7	-30.8	83.9	-21.6	-2.4	-12.5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
838	CTTAAATAGAGTCTCCCTTC SEQ.ID.IN:985	-6.7	-21.9	65.7	-15.2	0	-5.5
1034	GGGAGGCGGAGGCTGCAGTG SEQ.ID.IN:986	-6.7	-30.2	83.2	-22.2	-1.2	-8.9
1112	AAAATTAGCTGGGTATGGTG SEQ.ID.IN:987	-6.7	-20.1	60.6	-13.4	0	-4.8
1234	AGCACAGTGATTCATGCCTG SEQ.ID.IN:988	-6.7	-25.1	72.5	-17.2	-1.1	-7.6
1573	AAAGTTCCTTTGAGTGGCTG SEQ.ID.IN:989	-6.7	-23.1	68.2	-15.9	-0.1	-4.1
1753	TTTTTTTTTTTTTTTGGCAG SEQ.ID.IN:990	-6.7	-19.1	60.5	-12.4	0	-4
211	CACGTCGGGGTCGCTCCTGC SEQ.ID.IN:991	-6.6	-31.9	84	-24.4	-0.8	-6.5
382	CCGCAGCTTCCCCAGGTAGG SEQ.ID.IN:992	-6.6	-32.5	85.1	-25.9	0	-4.5
475	TCACAGGTGGCGGGCCGCTT SEQ.ID.IN:993	-6.6	-32	84.1	-22.8	-2.6	-10.8
969	CTCTGTCTTGGAAAAAAAAA SEQ.ID.IN:994	-6.6	-15	48.9	-8.4	0	-2.4
1318	TCCACAGAGAACTGGCAGGG SEQ.ID.IN:995	-6.6	-25.7	72.5	-17.4	-1.7	-6.9
1337	CCAAGACCCCAGCCTTGCTT SEQ.ID.IN:996	-6.6	-31.1	80.5	-23.4	-1	-4.8
1024	GGCTGCAGTGAGCCAGATTG SEQ.ID.IN:997	-6.5	-27.4	77.9	-18.3	-2.6	-11.9
1296	CCCCTGGCCTGGCCATCACA SEQ.ID.IN:998	-6.5	-34.5	87.4	-24.7	-2.5	-14.5
1730	CTTCCATTTAATGACTAAAA SEQ.ID.IN:999	-6.5	-16.6	52.4	-9.6	-0.1	-3.9
131	GCCTCACTTGGCCCGTGATG SEQ.ID.IN:1000	-6.4	-30.6	81	-22.7	-1.1	-10.5
1071	TACTCAGGAGGCTGAGGCGG SEQ.ID.IN:1001	-6.4	-27.2	76.6	-16.5	-4.3	-12.2
1179	TCACTTGAGGCCAGGAGTTC SEQ.ID.IN:1002	-6.4	-26.1	76.6	-19.2	0	-7.8
1276	GGGACTCACATGGGAGCCTT SEQ.ID.IN:1003	-6.4	-27.9	78.1	-19.5	-2	-10.4
1603	TCCAAACCTTGAAGATACTG SEQ.ID.IN:1004	-6.4	-20.2	59.3	-13.8	0	-2.8
1725	ATTTAATGACTAAAAATCAC SEQ.ID.IN:1005	-6.4	-13.1	45.6	-6.2	-0.1	-3.2
1731	ACTTCCATTTAATGACTAAA SEQ.ID.IN:1006	-6.4	-17.5	54.5	-11.1	0	-3.4
18	ATCTCTGGCCAGCGCAGCTC SEQ.ID.IN:1007	-6.3	-30.5	84.8	-21.6	-2.5	-12.5
431	AGGCGCAGGGGAGCTGGGCC SEQ.ID.IN:1008	-6.3	-33.4	88.9	-20.7	-6.4	-12.8
560	ATCTGGAAGGAACATCAAGT SEQ.ID.IN:1009	-6.3	-20	60.5	-13	-0.4	-3.6
572	GGGCCCACCACAATCTGGAA SEQ.ID.IN:1010	-6.3	-28.4	74.8	-19.3	-1.3	-13.7
648	ACACACGGGCACACACACAG SEQ.ID.IN:1011	-6.3	-25.3	69.6	-19	0	-4
708	AGCCACTTCGTGCAGGAATC SEQ.ID.IN:1012	-6.3	-26.1	73.5	-18.6	-0.7	-10.1
709	CAGCCACTTCGTGCAGGAAT SEQ.ID.IN:1013	-6.3	-26.4	73	-18.9	-0.7	-10.1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
792	GGGAGTGATGTTTTTGATGC SEQ.ID.IN:1014	-6.3	-22.8	68.8	-16.5	0	-2.6
1104	CTGGGTATGGTGATACGCGC SEQ.ID.IN:1015	-6.3	-26.3	72.8	-18.2	-1.8	-9.8
1150	CTGGGCAACATGGTGAACCC SEQ.ID.IN:1016	-6.3	-26.5	71.8	-19.3	-0.7	-8.3
1481	CTTCCTGTGGGCCCCTCCCA SEQ.ID.IN:1017	-6.3	-35.7	91.6	-26.6	-2.8	-10.2
500	TGGCCAAGGAGGCATCAGCT SEQ.ID.IN:1018	-6.2	-28.3	78.5	-18.7	-3.4	-10.4
644	ACGGGCACACACACAGGCCC SEQ.ID.IN:1019	-6.2	-30.5	79.4	-21.5	-2.8	-8.2
1026	GAGGCTGCAGTGAGCCAGAT SEQ.ID.IN:1020	-6.2	-27.9	79.4	-18.3	-3.4	-12.6
1144	AACATGGTGAACCCGTCTCT SEQ.ID.IN:1021	-6.2	-25.3	70	-19.1	0	-5.2
1180	ATCACTTGAGGCCAGGAGTT SEQ.ID.IN:1022	-6.2	-25.7	74.8	-19	0	-7.8
1363	TCACCCAGCTTCCACCATAC SEQ.ID.IN:1023	-6.2	-28.7	77.8	-22.5	0	-4.5
1441	AAGACTGCAGCAAAGACATC SEQ.ID.IN:1024	-6.2	-20.5	61.1	-13.6	0	-8.9
1476	TGTGGGCCCCTCCCACCCAC SEQ.ID.IN:1025	-6.2	-36.5	90.8	-25.5	-4.8	-10.7
2	GCTCAACTGTGGGTGTGATC SEQ.ID.IN:1026	-6.1	-25.2	74.6	-18.6	-0.1	-3.9
127	CACTTGGCCCGTGATGATGG SEQ.ID.IN:1027	-6.1	-27.3	73.6	-20.7	0	-8
309	ACAAAAGGGTTAGGACCCAG SEQ.ID.IN:1028	-6.1	-22.9	64.9	-12.7	-4.1	-9.2
339	ACGAGGAAGACCAGGAAGTG SEQ.ID.IN:1029	-6.1	-22.5	64.2	-15	-1.3	-5.1
529	GCCACGGCGGCTCTTGGCCC SEQ.ID.IN:1030	-6.1	-35.6	89.3	-27.2	-2.3	-11.3
793	AGGGAGTGATGTTTTTGATG SEQ.ID.IN:1031	-6.1	-21	64.6	-14.9	0	-1.1
1205	CACTTTGGGAGGCCGAGGCC SEQ.ID.IN:1032	-6.1	-30.4	80.9	-22.7	-1.4	-10.9
1297	TCCCCTGGCCTGGCCATCAC SEQ.ID.IN:1033	-6.1	-34.2	88.4	-25	-2.3	-14.3
1370	CCTTGGCTCACCCAGCTTCC SEQ.ID.IN:1034	-6.1	-32.1	86	-24.9	-1	-6
183	GGGCCTCCGTGTCTCAGGGC SEQ.ID.IN:1035	-6	-33.3	91.4	-25.3	-1.1	-12
364	GGCCACGGTGTGTGCCACAC SEQ.ID.IN:1036	-6	-31.1	83.1	-21.6	-3.5	-13.4
571	GGCCCACCACAATCTGGAAG SEQ.ID.IN:1037	-6	-27.2	72.8	-19.8	-1.3	-7.9
585	AAACCAGGACTCAGGGCCCA SEQ.ID.IN:1038	-6	-28.4	75.6	-20.8	-0.1	-11.3
641	GGCACACACACAGGCCCACT SEQ.ID.IN:1039	-6	-30.1	80.2	-23.1	-0.9	-6.8
757	GAAGGATTTTCTATCAATCT SEQ.ID.IN:1040	-6	-18.7	58.7	-11.7	-0.9	-4.4
992	CCAGCTTGGGCAACAGAGCA SEQ.ID.IN:1041	-6	-27.7	76.3	-19.2	-2.5	-7.9
16	CTCTGGCCAGCGCAGCTCAA SEQ.ID.IN:1042	-5.9	-30.1	81.3	-21.6	-2.5	-12.5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
775	TGCTCTGTTACTTTAGCTGA SEQ.ID.IN:1043	-5.9	-23.3	70.6	-16.2	-1.1	-4.8
842	GAATCTTAAATAGAGTCTCC SEQ.ID.IN:1044	-5.9	-18.8	58.7	-11.5	-1.3	-5.5
1718	GACTAAAAATCACACATCTC SEQ.ID.IN:1045	-5.9	-17.2	54.1	-11.3	0	-2.1
197	TCCTGCAATACTGGGGGCCT SEQ.ID.IN:1046	-5.8	-29.4	79.5	-23	0	-8.4
722	AAATGGTTCCCATCAGCCAC SEQ.ID.IN:1047	-5.8	-26	71.7	-18.6	-1.5	-6
774	GCTCTGTTACTTTAGCTGAA SEQ.ID.IN:1048	-5.8	-22.6	68.3	-16.1	-0.4	-4.8
1299	GGTCCCCTGGCCTGGCCATC SEQ.ID.IN:1049	-5.8	-35.7	93	-26.6	-2.5	-14.5
1339	ACCCAAGACCCCAGCCTTGC SEQ.ID.IN:1050	-5.8	-32.3	82.1	-25.4	-1	-4.3
1340	AACCCAAGACCCCAGCCTTG SEQ.ID.IN:1051	-5.8	-29.8	75.9	-23.1	-0.8	-4.2
1369	CTTGGCTCACCCAGCTTCCA SEQ.ID.IN:1052	-5.8	-30.8	83.6	-23.2	-1.8	-6
1701	CTCAGGTCACGGGTCTAGGA SEQ.ID.IN:1053	-5.8	-26.9	78	-21.1	0	-4
121	GCCCGTGATGATGGCCACCA SEQ.ID.IN:1054	-5.7	-31.6	80.7	-24.9	-0.8	-9.1
170	TCAGGGCATCCTCGGGGTTG SEQ.ID.IN:1055	-5.7	-29.4	81.5	-22.7	-0.9	-7.2
213	TCCACGTCGGGGTCGCTCCT SEQ.ID.IN:1056	-5.7	-32.5	85	-25.9	-0.8	-7.2
479	CTGGTCACAGGTGGCGGGCC SEQ.ID.IN:1057	-5.7	-31.7	85.9	-25.1	-0.8	-8.7
835	AAATAGAGTCTCCCTTCTCT SEQ.ID.IN:1058	-5.7	-23.4	69.5	-16.7	-0.9	-5.5
916	TGGGCCAGAATTTCTGGGGT SEQ.ID.IN:1059	-5.7	-27.1	76.3	-17.8	-3.6	-13.5
999	CTTCACTCCAGCTTGGGCAA SEQ.ID.IN:1060	-5.7	-27.3	76.6	-20	-1.6	-6.4
1025	AGGCTGCAGTGAGCCAGATT SEQ.ID.IN:1061	-5.7	-27.4	78.4	-18.3	-3.4	-12.6
1028	CGGAGGCTGCAGTGAGCCAG SEQ.ID.IN:1062	-5.7	-29.3	80.3	-20.2	-3.4	-12.6
1181	GATCACTTGAGGCCAGGAGT SEQ.ID.IN:1063	-5.7	-26.2	75.8	-20	0	-7.7
1477	CTGTGGGCCCCTCCCACCCA SEQ.ID.IN:1064	-5.7	-37.2	92	-26.7	-4.8	-10.7
1702	TCTCAGGTCACGGGTCTAGG SEQ.ID.IN:1065	-5.7	-26.7	78.5	-21	0	-4
169	CAGGGCATCCTCGGGGTTGG SEQ.ID.IN:1066	-5.6	-30.2	82.3	-23.6	-0.9	-6.9
938	CCAGGCTTGCCTCTAGATTG SEQ.ID.IN:1067	-5.6	-27.1	76.5	-19.9	-1.6	-8.9
1008	ATTGTACCACTTCACTCCAG SEQ.ID.IN:1068	-5.6	-24.4	70.9	-18.8	0	-4.2
1022	CTGCAGTGAGCCAGATTGTA SEQ.ID.IN:1069	-5.6	-25.3	73.7	-18.8	-0.8	-7.4
1287	TGGCCATCACAGGGACTCAC SEQ.ID.IN:1070	-5.6	-27.1	76.3	-20.8	-0.3	-8.7
1311	AGAACTGGCAGGGGTCCCCT SEQ.ID.IN:1071	-5.6	-30.8	83	-23.4	-1.8	-9.7

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
798	GGGAGAGGGAGTGATGTTTT SEQ.ID.IN:1072	-5.5	-23.9	71.7	-18.4	0	-1.1
1145	CAACATGGTGAACCCGTCTC SEQ.ID.IN:1073	-5.5	-25.1	69.3	-18.7	-0.7	-6.2
29	TGTGGGCAGGCATCTCTGGC SEQ.ID.IN:1074	-5.4	-29.4	84.3	-23.2	-0.6	-4.6
221	GGCAGCGTTCCACGTCGGGG SEQ.ID.IN:1075	-5.4	-31.7	82.9	-25.1	-1.1	-7.7
320	GCATCCAGGCGACAAAAGGG SEQ.ID.IN:1076	-5.4	-25.2	68.4	-19.8	0	-4.2
481	TGCTGGTCACAGGTGGCGGG SEQ.ID.IN:1077	-5.4	-29.7	82.3	-22.7	-1.5	-6.9
505	TCTGGTGGCCAAGGAGGCAT SEQ.ID.IN:1078	-5.4	-28.2	78.7	-19.4	-3.4	-8.5
1146	GCAACATGGTGAACCCGTCT SEQ.ID.IN:1079	-5.4	-26.5	71.7	-20.2	-0.7	-6.9
563	ACAATCTGGAAGGAACATCA SEQ.ID.IN:1080	-5.3	-19.7	59.1	-13.7	-0.4	-3.6
841	AATCTTAAATAGAGTCTCCC SEQ.ID.IN:1081	-5.3	-20.2	61.2	-14.4	-0.1	-5.5
1149	TGGGCAACATGGTGAACCCG SEQ.ID.IN:1082	-5.3	-26.4	70.1	-19.3	-1.8	-9.7
1294	CCTGGCCTGGCCATCACAGG SEQ.ID.IN:1083	-5.3	-31.7	83.9	-23.1	-2.5	-14.5
1480	TTCCTGTGGGCCCCTCCCAC SEQ.ID.IN:1084	-5.3	-35	90.4	-26	-3.7	-10.2
1485	TGAGCTTCCTGTGGGCCCCT SEQ.ID.IN:1085	-5.3	-33	88.2	-26.5	-0.1	-10.3
1646	CACACACACACACGGATTCC SEQ.ID.IN:1086	-5.3	-24.5	67.8	-19.2	0	-4.8
1735	AGACACTTCCATTTAATGAC SEQ.ID.IN:1087	-5.3	-19.8	60.1	-14.5	0	-3.9
193	GCAATACTGGGGGCCTCCGT SEQ.ID.IN:1088	-5.2	-30.5	80.8	-23.5	-1.1	-11.6
225	CTGAGGCAGCGTTCCACGTC SEQ.ID.IN:1089	-5.2	-28.8	79.2	-22.3	-1.2	-5.5
726	CTTGAAATGGTTCCCATCAG SEQ.ID.IN:1090	-5.2	-22.9	65.9	-16.1	-1.5	-6.2
797	GGAGAGGGAGTGATGTTTTT SEQ.ID.IN:1091	-5.2	-22.8	69.3	-17.6	0	-1.1
872	GCCCGGGATTCAGATGATCA SEQ.ID.IN:1092	-5.2	-27.1	74.2	-20.7	-0.5	-10.3
1107	TAGCTGGGTATGGTGATACG SEQ.ID.IN:1093	-5.2	-23.4	68.3	-16.4	-1.8	-7.6
1148	GGGCAACATGGTGAACCCGT SEQ.ID.IN:1094	-5.2	-27.6	73.2	-21.2	-1.1	-9.1
1411	GGCAAGGGAAGCGTCAGCGG SEQ.ID.IN:1095	-5.2	-28	75.2	-21.1	-1.7	-6.6
1413	ACGGCAAGGGAAGCGTCAGC SEQ.ID.IN:1096	-5.2	-27	73.4	-20.8	-0.9	-6
1537	GGTCCTCCACCCACTGCCCT SEQ.ID.IN:1097	-5.2	-35.5	91.1	-29.6	-0.4	-3.8
1648	CACACACACACACACGGATT SEQ.ID.IN:1098	-5.2	-23	64.6	-17.8	0	-3.5
294	CCCAGAAAGGAGTAGACGAA SEQ.ID.IN:1099	-5.1	-22.1	62.4	-16.5	-0.2	-3.7
562	CAATCTGGAAGGAACATCAA SEQ.ID.IN:1100	-5.1	-18.8	56.7	-13	-0.4	-3.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
993	TCCAGCTTGGGCAACAGAGC SEQ.ID.IN:1101	-5.1	-27.4	77	-20.7	-1.6	-6.6
1178	CACTTGAGGCCAGGAGTTCG SEQ.ID.IN:1102	-5.1	-26.5	74.6	-20.9	0	-7.8
1553	GTCACCCAAAGCTCCCGGTC SEQ.ID.IN:1103	-5.1	-30.5	80.4	-25.4	0	-6.2
579	GGACTCAGGGCCCACCACAA SEQ.ID.IN:1104	-5	-30	79.2	-23.3	-1.3	-11.3
621	GTGCCCAGAGACCCACACGC SEQ.ID.IN:1105	-5	-31.5	81.5	-25.8	-0.4	-4.1
640	GCACACACACAGGCCCACTG SEQ.ID.IN:1106	-5	-28.9	77.6	-22.6	-1.2	-6.8
653	TACACACACACGGGCACACA SEQ.ID.IN:1107	-5	-25	68.8	-20	0	-4
836	TAAATAGAGTCTCCCTTCTC SEQ.ID.IN:1108	-5	-22.2	66.9	-16.7	-0.1	-5.2
837	TTAAATAGAGTCTCCCTTCT SEQ.ID.IN:1109	-5	-21.9	65.7	-16.9	0	-5.5
893	TCTGAAAAGTCTGCATTCTT SEQ.ID.IN:1110	-5	-20.3	62	-14.6	-0.4	-6.2
966	TGTCTTGGAAAAAAAAAAAT SEQ.ID.IN:1111	-5	-11.4	42	-6.4	0	-2.6
982	CAACAGAGCAAGACTCTGTC SEQ.ID.IN:1112	-5	-21.9	65.5	-11.9	-5	-11.3
1270	CACATGGGAGCCTTTTAAAA SEQ.ID.IN:1113	-5	-21.2	61.4	-16.2	0	-6
1295	CCCTGGCCTGGCCATCACAG SEQ.ID.IN:1114	-5	-32.5	84.7	-24.2	-2.5	-14.5
1368	TTGGCTCACCCAGCTTCCAC SEQ.ID.IN:1115	-5	-30.1	82.3	-23.3	-1.8	-6
1533	CTCCACCCACTGCCCTTTGG SEQ.ID.IN:1116	-5	-32.1	83.2	-27.1	0	-3.4
1546	AAAGCTCCCGGTCCTCCACC SEQ.ID.IN:1117	-5	-31.5	81.2	-25.5	-0.9	-6.3
1736	CAGACACTTCCATTTAATGA SEQ.ID.IN:1118	-5	-20.3	60.8	-15.3	0	-3.9
72	CAGAGCAGGAAGGCCGGGAG SEQ.ID.IN:1119	-4.9	-27.7	75.3	-21.6	-1.1	-7.7
177	CCGTGTCTCAGGGCATCCTC SEQ.ID.IN:1120	-4.9	-30.2	84.3	-24.3	-0.9	-5
506	GTCTGGTGGCCAAGGAGGCA SEQ.ID.IN:1121	-4.9	-29.4	82.3	-21.1	-3.4	-9
620	TGCCCAGAGACCCACACGCG SEQ.ID.IN:1122	-4.9	-31.1	78	-26.2	0	-7.4
1105	GCTGGGTATGGTGATACGCG SEQ.ID.IN:1123	-4.9	-26.3	72.8	-20.3	-1	-7.6
1141	ATGGTGAACCCGTCTCTACT SEQ.ID.IN:1124	-4.9	-25.9	72.5	-20.1	-0.7	-5.4
1143	ACATGGTGAACCCGTCTCTA SEQ.ID.IN:1125	-4.9	-25.7	71.7	-19.9	-0.7	-5.3
1277	AGGGACTCACATGGGAGCCT SEQ.ID.IN:1126	-4.9	-27.8	78	-20.9	-2	-10.4
1544	AGCTCCCGGTCCTCCACCCA SEQ.ID.IN:1127	-4.9	-35.6	90.3	-29.7	-0.9	-5.7
116	TGATGATGGCCACCACGTAC SEQ.ID.IN:1128	-4.8	-25.9	70.8	-20.2	-0.6	-9.1
135	CGCAGCCTCACTTGGCCCGT SEQ.ID.IN:1129	-4.8	-33.3	85	-26.6	-1.9	-7.1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	TCTCCATGTCGTTCCGGTGG						
248	SEQ.ID.IN:1130	-4.8	-28.9	79.7	-23.5	-0.3	-6.6
	GGGTAGATGGTCTCCATGTC						
258	SEQ.ID.IN:1131	-4.8	-26.3	78.4	-19.9	-1.6	-6.5
	CCAGGCGACAAAAGGGTTAG						
316	SEQ.ID.IN:1132	-4.8	-23.3	65.1	-18.5	0	-4
	AACCAGGACTCAGGGCCCAC						
584	SEQ.ID.IN:1133	-4.8	-29.3	78.5	-22.9	0.1	-11.3
	CGCGCAGCAGGCTGCCAGGA						
604	SEQ.ID.IN:1134	-4.8	-32.6	84.3	-24.9	-2.7	-13.5
	GTGCAGGAATCCAAGGGGCT						
699	SEQ.ID.IN:1135	-4.8	-27.5	76.3	-22.2	-0.1	-6.1
	AGCCTCACTTGGCCCGTGAT						
132	SEQ.ID.IN:1136	-4.7	-30.6	81.5	-24	-1.9	-10.5
	CTCTTGGCCCATGGTCTGGT						
519	SEQ.ID.IN:1137	-4.7	-30.1	84.3	-24.4	-0.9	-7.9
	GGGCACACACAGGCCCAC						
642	SEQ.ID.IN:1138	-4.7	-30.4	80.8	-22.3	-3.4	-9.4
	CATGGTGAACCCGTCTCTAC						
1142	SEQ.ID.IN:1139	-4.7	-25.7	71.7	-20.1	-0.7	-5.3
	AAGCTCCCGGTCCTCCACCC						
1545	SEQ.ID.IN:1140	-4.7	-34.2	86.8	-28.5	-0.9	-6.3
	GAAAGTTCCTTTGAGTGGCT						
1574	SEQ.ID.IN:1141	-4.7	-23.7	69.7	-18.1	-0.7	-4.7
	GGGGTCGCTCCTGCAATACT						
205	SEQ.ID.IN:1142	-4.6	-28.6	78.5	-22.6	-1.3	-6.4
	TCCCAGAGGATCTGCAGAGC						
456	SEQ.ID.IN:1143	-4.6	-27.7	78.8	-20.6	-2.4	-12.5
	TCCCAGCTACTCAGGAGGCT						
1078	SEQ.ID.IN:1144	-4.6	-29.4	82.7	-24.2	-0.3	-5.7
	CAGCACTTTGGGAGGCCGAG						
1208	SEQ.ID.IN:1145	-4.6	-27.9	76.3	-22	-1.2	-7.7
	AGAGGAGCCAGCCCTGTCCT						
1387	SEQ.ID.IN:1146	-4.6	-32.1	87.2	-26.4	-1	-8.1
	CACACACACGGGCACACACA						
651	SEQ.ID.IN:1147	-4.5	-26	70.4	-21.5	0	-4
	CTAAAAATACAAAAATTAGC						
1123	SEQ.ID.IN:1148	-4.5	-11.2	41.7	-6.7	0	-3.2
	CCAGCCCTGTCCTTGGCTCA						
1380	SEQ.ID.IN:1149	-4.5	-33	88.4	-26.3	-2.2	-6.6
	GAGGAGCCAGCCCTGTCCTT						
1386	SEQ.ID.IN:1150	-4.5	-32.2	87.3	-26.4	-1.2	-8.3
	CTTGATGACCAGCAGCGTGC						
94	SEQ.ID.IN:1151	-4.4	-27.2	75.3	-21.6	-1.1	-7.2
	GTGGCGGGCCGCTTCCCAGA						
469	SEQ.ID.IN:1152	-4.4	-34.5	87.8	-27.5	-2.6	-11.2
	TGGTCACAGGTGGCGGGCCG						
478	SEQ.ID.IN:1153	-4.4	-31.6	83.4	-25.8	-1.3	-8.5
	AATCTGGAAGGAACATCAAG						
561	SEQ.ID.IN:1154	-4.4	-18.1	55.7	-13	-0.4	-3.6
	CACAATCTGGAAGGAACATC						
564	SEQ.ID.IN:1155	-4.4	-19.7	59.1	-15.3	0.1	-4
	GGAAACCAGGACTCAGGGCC						
587	SEQ.ID.IN:1156	-4.4	-27.5	74.9	-23.1	0	-6.4
	CCAGGAAACCAGGACTCAGG						
590	SEQ.ID.IN:1157	-4.4	-25.2	69.8	-20.2	-0.3	-4.4
	ACACACACACGGGCACACAC						
652	SEQ.ID.IN:1158	-4.4	-25.5	69.8	-21.1	0	-4

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
917	CTGGGCCAGAATTTCTGGGG SEQ.ID.IN:1159	-4.4	-26.8	74.8	-19.5	-2.9	-12.8
1291	GGCCTGGCCATCACAGGGAC SEQ.ID.IN:1160	-4.4	-30.8	83.3	-23.6	-2.5	-13.3
1555	TGGTCACCCAAAGCTCCCGG SEQ.ID.IN:1161	-4.4	-30.1	77.7	-24.8	-0.8	-7.3
21	GGCATCTCTGGCCAGCGCAG SEQ.ID.IN:1162	-4.3	-31.1	84.5	-24.6	-1.8	-12.3
310	GACAAAAGGGTTAGGACCCA SEQ.ID.IN:1163	-4.3	-23.5	65.9	-15.1	-4.1	-9.2
363	GCCACGGTGTGTGCCACACG SEQ.ID.IN:1164	-4.3	-30.7	80.1	-22.1	-4.3	-13.4
508	TGGTCTGGTGGCCAAGGAGG SEQ.ID.IN:1165	-4.3	-28.1	79.2	-22.2	-1.6	-9
603	GCGCAGCAGGCTGCCAGGAA SEQ.ID.IN:1166	-4.3	-31.1	82.4	-23.7	-2.5	-14.1
990	AGCTTGGGCAACAGAGCAAG SEQ.ID.IN:1167	-4.3	-24.3	69.6	-17.5	-2.5	-7.9
1280	CACAGGGACTCACATGGGAG SEQ.ID.IN:1168	-4.3	-24.7	70.9	-19.7	-0.3	-8
1310	GAACTGGCAGGGGTCCCCTG SEQ.ID.IN:1169	-4.3	-30.8	82.4	-22.8	-3.7	-13.6
1385	AGGAGCCAGCCCTGTCCTTG SEQ.ID.IN:1170	-4.3	-31.6	85.7	-26.4	-0.7	-7.4
1647	ACACACACACACACGGATTC SEQ.ID.IN:1171	-4.3	-22.7	64.9	-18.4	0	-3.5
120	CCCGTGATGATGGCCACCAC SEQ.ID.IN:1172	-4.2	-30	77.3	-24.9	-0.6	-9.1
589	CAGGAAACCAGGACTCAGGG SEQ.ID.IN:1173	-4.2	-24.4	68.7	-19.6	-0.3	-4.4
643	CGGGCACACACACAGGCCCA SEQ.ID.IN:1174	-4.2	-31	79.8	-22.9	-3.9	-9.6
654	ATACACACACACGGGCACAC SEQ.ID.IN:1175	-4.2	-24.3	67.7	-20.1	0	-4
794	GAGGGAGTGATGTTTTTGAT SEQ.ID.IN:1176	-4.2	-21.6	66.1	-17.4	0	-1.3
1406	GGGAAGCGTCAGCGGGGGCA SEQ.ID.IN:1177	-4.2	-31.1	82.2	-25.8	-1	-6.8
1644	CACACACACACGGATTCCCC SEQ.ID.IN:1178	-4.2	-27.6	72.9	-23.4	0	-5.2
198	CTCCTGCAATACTGGGGGCC SEQ.ID.IN:1179	-4.1	-29.4	79.5	-24.7	0	-8.4
340	CACGAGGAAGACCAGGAAGT SEQ.ID.IN:1180	-4.1	-23.2	65.4	-18.4	-0.5	-5.1
470	GGTGGCGGGCCGCTTCCCAG SEQ.ID.IN:1181	-4.1	-35.1	89	-28.4	-2.6	-10.9
520	GCTCTTGGCCCATGGTCTGG SEQ.ID.IN:1182	-4.1	-30.7	85.1	-25.7	-0.6	-9.3
1182	GGATCACTTGAGGCCAGGAG SEQ.ID.IN:1183	-4.1	-26.2	74.9	-21.6	0	-7.7
196	CCTGCAATACTGGGGGCCTC SEQ.ID.IN:1184	-4	-29.4	79.5	-24.9	0	-7.5
365	AGGCCACGGTGTGTGCCACA SEQ.ID.IN:1185	-4	-30.9	82.8	-22.6	-4.3	-11.9
471	AGGTGGCGGGCCGCTTCCCA SEQ.ID.IN:1186	-4	-35.1	89	-28.3	-2.8	-11
659	TACACATACACACACACGGG SEQ.ID.IN:1187	-4	-22.2	63.3	-18.2	0	-3.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1136	GAACCCGTCTCTACTAAAAA SEQ.ID.IN:1188	-4	-20.4	58.8	-16.4	0	-2.2
1293	CTGGCCTGGCCATCACAGGG SEQ.ID.IN:1189	-4	-30.9	83.1	-23.6	-2.5	-14.5
1628	CCCCATCAAGGGGACATTTG SEQ.ID.IN:1190	-4	-26.4	71.7	-19.1	-3.3	-8.4
1679	AAACACACACACACACACAC SEQ.ID.IN:1191	-4	-20	58.7	-16	0	0
1729	TTCCATTTAATGACTAAAAA SEQ.ID.IN:1192	-4	-15	49	-11	0.1	-3.9
174	TGTCTCAGGGCATCCTCGGG SEQ.ID.IN:1193	-3.9	-29.4	82.4	-24.5	-0.9	-4.8
437	CCATGGAGGCGCAGGGGAGC SEQ.ID.IN:1194	-3.9	-30.8	82.3	-26.2	-0.4	-8.4
73	GCAGAGCAGGAAGGCCGGGA SEQ.ID.IN:1195	-3.8	-29.5	79.2	-24.5	-1.1	-7.7
126	ACTTGGCCCGTGATGATGGC SEQ.ID.IN:1196	-3.8	-28.4	76.6	-23.9	-0.4	-6.6
570	GCCCACCACAATCTGGAAGG SEQ.ID.IN:1197	-3.8	-27.2	72.8	-22	-1.3	-6.4
639	CACACACACAGGCCCACTGT SEQ.ID.IN:1198	-3.8	-28.3	76.7	-22.6	-1.9	-6.8
1079	ATCCCAGCTACTCAGGAGGC SEQ.ID.IN:1199	-3.8	-28.5	80.6	-24.2	-0.2	-5.2
1292	TGGCCTGGCCATCACAGGGA SEQ.ID.IN:1200	-3.8	-30.6	82.5	-23.6	-2.5	-14.3
226	CCTGAGGCAGCGTTCCACGT SEQ.ID.IN:1201	-3.7	-30.4	80.8	-24.9	-1.8	-6.3
433	GGAGGCGCAGGGGAGCTGGG SEQ.ID.IN:1202	-3.7	-31.4	85	-26.2	-1.4	-8.4
509	ATGGTCTGGTGGCCAAGGAG SEQ.ID.IN:1203	-3.7	-26.9	76.5	-21.2	-2	-9
658	ACACATACACACACACGGGC SEQ.ID.IN:1204	-3.7	-24.3	67.7	-20.6	0	-3.5
770	TGTTACTTTAGCTGAAGGAT SEQ.ID.IN:1205	-3.7	-20.4	62.6	-16.2	0.5	-8.4
834	AATAGAGTCTCCCTTCTCTC SEQ.ID.IN:1206	-3.7	-24.5	73.7	-19.6	-1.1	-5.5
967	CTGTCTTGGAAAAAAAAAAA SEQ.ID.IN:1207	-3.7	-12.3	43.6	-8.6	0	-2.6
1147	GGCAACATGGTGAACCCGTC SEQ.ID.IN:1208	-3.7	-26.8	72.3	-22.2	-0.7	-6.9
1317	CCACAGAGAACTGGCAGGGG SEQ.ID.IN:1209	-3.7	-26.5	73.4	-21.1	-1.7	-6.8
1334	AGACCCCAGCCTTGCTTCCA SEQ.ID.IN:1210	-3.7	-32.2	84.7	-27.8	-0.5	-4.2
117	GTGATGATGGCCACCACGTA SEQ.ID.IN:1211	-3.6	-26.9	73.4	-22.4	-0.6	-9.1
133	CAGCCTCACTTGGCCCGTGA SEQ.ID.IN:1212	-3.6	-31.3	82.5	-25.8	-1.9	-10
434	TGGAGGCGCAGGGGAGCTGG SEQ.ID.IN:1213	-3.6	-30.2	82.2	-25.1	-1.4	-7.6
758	TGAAGGATTTTCTATCAATC SEQ.ID.IN:1214	-3.6	-17.8	56.7	-13.3	-0.8	-5.1
1183	TGGATCACTTGAGGCCAGGA SEQ.ID.IN:1215	-3.6	-26.2	74.4	-22.1	0	-7.7
1586	CTGAAGGGACCAGAAAGTTC SEQ.ID.IN:1216	-3.6	-21.6	63.4	-18	0	-4.5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
164	CATCCTCGGGGTTGGCAAAG SEQ.ID.IN:1217	-3.5	-26.4	72.4	-22.4	-0.2	-7
212	CCACGTCGGGGTCGCTCCTG SEQ.ID.IN:1218	-3.5	-32.1	83.1	-27.7	-0.8	-7.2
647	CACACGGGCACACACACAGG SEQ.ID.IN:1219	-3.5	-26.3	71.4	-22.8	0	-4
1184	GTGGATCACTTGAGGCCAGG SEQ.ID.IN:1220	-3.5	-26.8	76.5	-22.6	-0.4	-8.3
455	CCCAGAGGATCTGCAGAGCC SEQ.ID.IN:1221	-3.4	-29.3	80.5	-22.8	-2.4	-14.1
723	GAAATGGTTCCCATCAGCCA SEQ.ID.IN:1222	-3.4	-26.4	72.4	-21.4	-1.5	-6
1096	GGTGATACGCGCCTGTAATC SEQ.ID.IN:1223	-3.4	-25.6	70.8	-21.1	-1	-7.7
1135	AACCCGTCTCTACTAAAAAT SEQ.ID.IN:1224	-3.4	-19.8	57.7	-16.4	0	-2.6
1204	ACTTTGGGAGGCCGAGGCCG SEQ.ID.IN:1225	-3.4	-30.5	79.5	-24.5	-2.5	-12.2
1414	AACGGCAAGGGAAGCGTCAG SEQ.ID.IN:1226	-3.4	-24.5	67.3	-20.1	-0.9	-6
1643	ACACACACACGGATTCCCCA SEQ.ID.IN:1227	-3.4	-27.6	72.9	-23.4	-0.6	-5.2
566	ACCACAATCTGGAAGGAACA SEQ.ID.IN:1228	-3.3	-21.5	61.8	-16.8	-1.3	-5.4
567	CACCACAATCTGGAAGGAAC SEQ.ID.IN:1229	-3.3	-21.5	61.8	-16.8	-1.3	-5.4
777	GATGCTCTGTTACTTTAGCT SEQ.ID.IN:1230	-3.3	-23.3	70.8	-18.8	-1.1	-4.5
991	CAGCTTGGGCAACAGAGCAA SEQ.ID.IN:1231	-3.3	-25	70.4	-19.2	-2.5	-7.9
1532	TCCACCCACTGCCCTTTGGA SEQ.ID.IN:1232	-3.3	-31.8	82.6	-27.9	-0.3	-5.8
1538	CGGTCCTCCACCCACTGCCC SEQ.ID.IN:1233	-3.3	-35.4	88.4	-31.1	-0.9	-4.3
1548	CCAAAGCTCCCGGTCCTCCA SEQ.ID.IN:1234	-3.3	-32	81.5	-27.7	-0.9	-6.2
501	GTGGCCAAGGAGGCATCAGC SEQ.ID.IN:1235	-3.2	-28.6	80.1	-22	-3.4	-10.2
510	CATGGTCTGGTGGCCAAGGA SEQ.ID.IN:1236	-3.2	-27.6	77.2	-22.4	-2	-9.2
725	TTGAAATGGTTCCCATCAGC SEQ.ID.IN:1237	-3.2	-23.8	68.1	-19.5	-1	-6.2
892	CTGAAAAGTCTGCATTCTTA SEQ.ID.IN:1238	-3.2	-19.6	60	-15.9	-0.2	-6.1
1300	GGGTCCCCTGGCCTGGCCAT SEQ.ID.IN:1239	-3.2	-36.5	93.5	-30	-2.5	-14.5
1384	GGAGCCAGCCCTGTCCTTGG SEQ.ID.IN:1240	-3.2	-32.8	87.8	-29.1	-0.1	-5.9
1645	ACACACACACACGGATTCCC SEQ.ID.IN:1241	-3.2	-25.8	70.1	-22.6	0	-5.2
1700	TCAGGTCACGGGTCTAGGAG SEQ.ID.IN:1242	-3.2	-26	76.3	-22.8	0	-4
24	GCAGGCATCTCTGGCCAGCG SEQ.ID.IN:1243	-3.1	-31.1	84.5	-24.9	-3.1	-11.9
518	TCTTGGCCCATGGTCTGGTG SEQ.ID.IN:1244	-3.1	-29.2	82	-25.1	-0.9	-7.9
1138	GTGAACCCGTCTCTACTAAA SEQ.ID.IN:1245	-3.1	-23	65.3	-19.9	0	-2.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	ACAGGGACTCACATGGGAGC						
1279	SEQ.ID.IN:1246	-3.1	-25.8	74.1	-22	-0.4	-8.2
	GAGCCAGCCCTGTCCTTGGC						
1383	SEQ.ID.IN:1247	-3.1	-33.4	89.8	-27.9	-2.4	-7.4
	CAAAGCTCCCGGTCCTCCAC						
1547	SEQ.ID.IN:1248	-3.1	-30.2	78.9	-26.1	-0.9	-6.2
	TCCGTGTCTCAGGGCATCCT						
178	SEQ.ID.IN:1249	-3	-30.2	84.3	-26.1	-1	-5.6
	GTTACTTTAGCTGAAGGATT						
769	SEQ.ID.IN:1250	-3	-20.5	63.1	-16.6	-0.4	-9.3
	GGCTGGGCCAGAATTTCTGG						
919	SEQ.ID.IN:1251	-3	-27.4	76.5	-21.2	-3.2	-12.8
	CACGGCGGCTCTTGGCCCAT						
527	SEQ.ID.IN:1252	-2.9	-32.5	83	-27.3	-2.3	-7.7
	ACGCGCAGCAGGCTGCCAGG						
605	SEQ.ID.IN:1253	-2.9	-32.2	83.7	-26.1	-2.7	-14.2
	ATGCTCTGTTACTTTAGCTG						
776	SEQ.ID.IN:1254	-2.9	-22.7	69.2	-18.6	-1.1	-4.8
	AGTCTGCATTCTTAGCCCGG						
886	SEQ.ID.IN:1255	-2.9	-28	78.3	-25.1	0.6	-6.4
	CCTGTAATCCCAGCTACTCA						
1085	SEQ.ID.IN:1256	-2.9	-26.8	74.7	-23.9	0	-4.6
	AGGGAAGCGTCAGCGGGGGC						
1407	SEQ.ID.IN:1257	-2.9	-30.4	81.6	-25.8	-1.7	-6
	ACACACACGGATTCCCCATC						
1641	SEQ.ID.IN:1258	-2.9	-27.1	72.8	-23.4	-0.6	-5.2
	CAGAGGATCTGCAGAGCCAT						
453	SEQ.ID.IN:1259	-2.8	-26	74.4	-21.2	-1.9	-11.1
	TTCCCAGAGGATCTGCAGAG						
457	SEQ.ID.IN:1260	-2.8	-26	74.7	-20.6	-2.4	-12.6
	TTCACTCCAGCTTGGGCAAC						
998	SEQ.ID.IN:1261	-2.8	-26.6	75.3	-22.2	-1.6	-6.4
	GCGTCAGCGGGGGCAGAGGA						
1401	SEQ.ID.IN:1262	-2.8	-31.2	84	-27.3	-1	-5.9
	GTTCCACGTCGGGGTCGCTC						
215	SEQ.ID.IN:1263	-2.7	-30.9	83.8	-27.5	-0.4	-6.6
	CATGGAGGCGCAGGGGAGCT						
436	SEQ.ID.IN:1264	-2.7	-29.7	80.8	-26.2	-0.6	-8.4
	TGGCGGGCCGCTTCCCAGAG						
468	SEQ.ID.IN:1265	-2.7	-33.3	84.8	-28	-2.6	-11.2
	ACACGGGCACACACACAGGC						
646	SEQ.ID.IN:1266	-2.7	-27.4	74.4	-24.7	0	-4
	CTACTCAGGAGGCTGAGGCG						
1072	SEQ.ID.IN:1267	-2.7	-26.9	76	-19.9	-4.3	-12
	CCCAGCTACTCAGGAGGCTG						
1077	SEQ.ID.IN:1268	-2.7	-29	80.6	-24.2	-2.1	-9.3
	TGATTCATGCCTGTCATCCC						
1227	SEQ.ID.IN:1269	-2.7	-27.2	76.5	-24.5	0	-4
	AGCCAGCCCTGTCCTTGGCT						
1382	SEQ.ID.IN:1270	-2.7	-33.7	90.4	-27.8	-3.2	-8.7
	AGCGTCAGCGGGGGCAGAGG						
1402	SEQ.ID.IN:1271	-2.7	-30.6	83	-26.1	-1.8	-6.6
	CCACCCACTGCCCTTTGGAG						
1531	SEQ.ID.IN:1272	-2.7	-31.4	81.3	-28.1	-0.3	-4.9
	AGAGGATCTGCAGAGCCATG						
452	SEQ.ID.IN:1273	-2.6	-25.3	73.1	-21.2	3.4	-11.1
	CGCTTCCCAGAGGATCTGCA						
460	SEQ.ID.IN:1274	-2.6	-28.9	78.7	-23.9	-2.4	-7.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
764	TTTAGCTGAAGGATTTTCTA SEQ.ID.IN:1275	-2.6	-19.6	61.1	-16.1	-0.8	-7
766	ACTTTAGCTGAAGGATTTTC SEQ.ID.IN:1276	-2.6	-20.1	62.3	-16.6	-0.4	-9.3
918	GCTGGGCCAGAATTTCTGGG SEQ.ID.IN:1277	-2.6	-27.4	76.5	-21.2	-3.6	-13.5
920	TGGCTGGGCCAGAATTTCTG SEQ.ID.IN:1278	-2.6	-26.2	73.8	-21.2	-2.4	-9.6
1541	TCCCGGTCCTCCACCCACTG SEQ.ID.IN:1279	-2.6	-34	86.1	-30.4	-0.9	-6.2
1587	ACTGAAGGGACCAGAAAGTT SEQ.ID.IN:1280	-2.6	-21.4	62.6	-18	-0.6	-4.5
921	TTGGCTGGGCCAGAATTTCT SEQ.ID.IN:1281	-2.5	-26.3	74.3	-21.2	-2.6	-12.1
1084	CTGTAATCCCAGCTACTCAG SEQ.ID.IN:1282	-2.5	-24.8	71.4	-22.3	0	-4.6
1699	CAGGTCACGGGTCTAGGAGA SEQ.ID.IN:1283	-2.5	-26.2	75.9	-23.7	0	-4
444	TGCAGAGCCATGGAGGCGCA SEQ.ID.IN:1284	-2.4	-29.7	79.9	-23.9	-3.4	-10.6
472	CAGGTGGCGGGCCGCTTCCC SEQ.ID.IN:1285	-2.4	-35.1	89	-30.1	-2.6	-10.8
578	GACTCAGGGCCCACCACAAT SEQ.ID.IN:1286	-2.4	-28.8	76.8	-24.7	-1.3	-11.3
773	CTCTGTTACTTTAGCTGAAG SEQ.ID.IN:1287	-2.4	-20.8	64.2	-17.7	0	-8.8
1101	GGTATGGTGATACGCGCCTG SEQ.ID.IN:1288	-2.4	-27.1	73.8	-22.9	-1.8	-9.8
1137	TGAACCCGTCTCTACTAAAA SEQ.ID.IN:1289	-2.4	-21.1	60.5	-18.7	0	-2.6
1642	CACACACACGGATTCCCCAT SEQ.ID.IN:1290	-2.4	-27.4	72.3	-24.2	-0.6	-5.2
9	CAGCGCAGCTCAACTGTGGG SEQ.ID.IN:1291	-2.3	-27.6	76.3	-22.8	-2.5	-8.5
118	CGTGATGATGGCCACCACGT SEQ.ID.IN:1292	-2.3	-28	73.8	-23.9	0.9	-11.8
461	CCGCTTCCCAGAGGATCTGC SEQ.ID.IN:1293	-2.3	-30.2	81.1	-25.5	-2.4	-7.8
619	GCCCAGAGACCCACACGCGC SEQ.ID.IN:1294	-2.3	-32.9	82	-30.1	0	-7.7
796	GAGAGGGAGTGATGTTTTTG SEQ.ID.IN:1295	-2.3	-21.6	66.4	-19.3	0	-1.1
968	TCTGTCTTGGAAAAAAAAAA SEQ.ID.IN:1296	-2.3	-13.4	45.8	-11.1	0	-2.6
1379	CAGCCCTGTCCTTGGCTCAC SEQ.ID.IN:1297	-2.3	-31.2	85.6	-26.7	-2.2	-6.6
1381	GCCAGCCCTGTCCTTGGCTC SEQ.ID.IN:1298	-2.3	-34.1	92	-29.4	-2.4	-7.7
1405	GGAAGCGTCAGCGGGGGCAG SEQ.ID.IN:1299	-2.3	-29.9	80.1	-25.8	-1.8	-6.6
1491	GAAGGCTGAGCTTCCTGTGG SEQ.ID.IN:1300	-2.3	-26.9	76.8	-23.7	-0.8	-6.5
1575	AGAAAGTTCCTTTGAGTGGC SEQ.ID.IN:1301	-2.3	-22.8	67.9	-19.6	-0.7	-4.1
91	GATGACCAGCAGCGTGCTGC SEQ.ID.IN:1302	-2.2	-28.9	79.2	-22.8	-3.8	-14.8
134	GCAGCCTCACTTGGCCCGTG SEQ.ID.IN:1303	-2.2	-32.5	85.5	-28.4	-1.9	-8.4

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
480	GCTGGTCACAGGTGGCGGGC SEQ.ID.IN:1304	-2.2	-31.5	87.1	-27.7	-1.5	-8.2
630	AGGCCCACTGTGCCCAGAGA SEQ.ID.IN:1305	-2.2	-31.7	84.4	-27.8	-1.7	-9.1
1585	TGAAGGGACCAGAAAGTTCC SEQ.ID.IN:1306	-2.2	-22.7	65.2	-20	-0.2	-4.4
1588	TACTGAAGGGACCAGAAAGT SEQ.ID.IN:1307	-2.2	-21	61.7	-18	-0.6	-4.5
90	ATGACCAGCAGCGTGCTGCA SEQ.ID.IN:1308	-2.1	-29	78.9	-22.8	-3.5	-16.1
1124	ACTAAAAATACAAAAATTAG SEQ.ID.IN:1309	-2.1	-9.6	38.9	-7.5	0	-3.5
1139	GGTGAACCCGTCTCTACTAA SEQ.ID.IN:1310	-2.1	-24.9	69.9	-22.8	0	-5.1
1186	CGGTGGATCACTTGAGGCCA SEQ.ID.IN:1311	-2.1	-27.6	76	-24.3	-1.1	-9.2
1540	CCCGGTCCTCCACCCACTGC SEQ.ID.IN:1312	-2.1	-35.4	88.4	-32.3	-0.9	-6.2
459	GCTTCCCAGAGGATCTGCAG SEQ.ID.IN:1313	-2	-28.1	79.5	-23.7	-2.4	-9.8
514	GGCCCATGGTCTGGTGGCCA SEQ.ID.IN:1314	-2	-33.5	89.5	-28.4	-3.1	-10.8
698	TGCAGGAATCCAAGGGGCTA SEQ.ID.IN:1315	-2	-26	72.4	-23.4	-0.3	-6.9
1177	ACTTGAGGCCAGGAGTTCGA SEQ.ID.IN:1316	-2	-26.4	74.8	-23.9	0	-7.7
1498	GGGAGGAGAAGGCTGAGCTT SEQ.ID.IN:1317	-2	-26	74.9	-23.3	-0.4	-6
1552	TCACCCAAAGCTCCCGGTCC SEQ.ID.IN:1318	-2	-31.3	80.3	-29.3	0	-6.2
247	CTCCATGTCGTTCCGGTGGG SEQ.ID.IN:1319	-1.9	-29.7	80.5	-26.9	-0.7	-6.6
458	CTTCCCAGAGGATCTGCAGA SEQ.ID.IN:1320	-1.9	-26.9	76.4	-22.7	-1.9	-12.5
767	TACTTTAGCTGAAGGATTTT SEQ.ID.IN:1321	-1.9	-19.4	60.3	-16.6	-0.4	-9.3
768	TTACTTTAGCTGAAGGATTT SEQ.ID.IN:1322	-1.9	-19.4	60.3	-16.6	-0.4	-9.3
994	CTCCAGCTTGGGCAACAGAG SEQ.ID.IN:1323	-1.9	-26.5	74.6	-23.6	-0.9	-6.4
1086	GCCTGTAATCCCAGCTACTC SEQ.ID.IN:1324	-1.9	-27.9	77.9	-26	0	-4.6
1486	CTGAGCTTCCTGTGGGCCCC SEQ.ID.IN:1325	-1.9	-33	88.2	-29.9	-0.1	-10.3
1499	TGGGAGGAGAAGGCTGAGCT SEQ.ID.IN:1326	-1.9	-25.9	74.3	-23.3	-0.4	-5
125	CTTGGCCCGTGATGATGGCC SEQ.ID.IN:1327	-1.8	-30.2	79.4	-25.5	-2.9	-8.3
224	TGAGGCAGCGTTCCACGTCG SEQ.ID.IN:1328	-1.8	-28.7	77	-25.6	-1.2	-8.4
366	TAGGCCACGGTGTGTGCCAC SEQ.ID.IN:1329	-1.8	-29.9	81.3	-23.8	-4.3	-11.9
447	ATCTGCAGAGCCATGGAGGC SEQ.ID.IN:1330	-1.8	-27.7	78.5	-23.3	-2.3	-13
588	AGGAAACCAGGACTCAGGGC SEQ.ID.IN:1331	-1.8	-25.5	71.7	-23.1	-0.3	-4.4
628	GCCCACTGTGCCCAGAGACC SEQ.ID.IN:1332	-1.8	-32.7	85.4	-30.2	-0.4	-6.3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
660	ATACACATACACACACACGG SEQ.ID.IN:1333	-1.8	-21	60.9	-19.2	0	-3.5
1174	TGAGGCCAGGAGTTCGAGAC SEQ.ID.IN:1334	-1.8	-26	74.1	-23.7	0	-7.7
1187	CCGGTGGATCACTTGAGGCC SEQ.ID.IN:1335	-1.8	-28.9	78.3	-25.9	-1.1	-7.9
1410	GCAAGGGAAGCGTCAGCGGG SEQ.ID.IN:1336	-1.8	-28	75.2	-24.5	-1.7	-6.2
1598	ACCTTGAAGATACTGAAGGG SEQ.ID.IN:1337	-1.8	-20.8	61.4	-17.5	-1.4	-6.4
1698	AGGTCACGGGTCTAGGAGAA SEQ.ID.IN:1338	-1.8	-24.8	72.2	-23	0	-4
216	CGTTCCACGTCGGGGTCGCT SEQ.ID.IN:1339	-1.7	-31.3	81.4	-27	-2.6	-6.6
435	ATGGAGGCGCAGGGGAGCTG SEQ.ID.IN:1340	-1.7	-29	79.6	-26.2	-1	-8.4
577	ACTCAGGGCCCACCACAATC SEQ.ID.IN:1341	-1.7	-28.6	77.1	-25.3	-1.3	-10.5
580	AGGACTCAGGGCCCACCACA SEQ.ID.IN:1342	-1.7	-30.7	82	-27.3	-1.3	-11.3
675	AACATACACACACACATACA SEQ.ID.IN:1343	-1.7	-19	57.2	-17.3	0	-0.9
1097	TGGTGATACGCGCCTGTAAT SEQ.ID.IN:1344	-1.7	-25.2	69.2	-21.8	-1.7	-7.8
1100	GTATGGTGATACGCGCCTGT SEQ.ID.IN:1345	-1.7	-27.1	74.5	-23.7	-1.7	-9.8
1191	GAGGCCGGTGGATCACTTGA SEQ.ID.IN:1346	-1.7	-27.5	76.2	-24.6	-1.1	-9
1207	AGCACTTTGGGAGGCCGAGG SEQ.ID.IN:1347	-1.7	-28.4	77.8	-25.4	-1.2	-7.7
1502	CCTTGGGAGGAGAAGGCTGA SEQ.ID.IN:1348	-1.7	-26.2	73.7	-23.6	-0.7	-5.1
44	TGCTCATCACCAGGCTGTGG SEQ.ID.IN:1349	-1.6	-28.1	79.6	-25.3	-1.1	-5.8
656	ACATACACACACACGGGCAC SEQ.ID.IN:1350	-1.6	-24.3	67.7	-22.7	0	-4
1590	GATACTGAAGGGACCAGAAA SEQ.ID.IN:1351	-1.6	-20.4	59.9	-18	-0.6	-4.5
10	CCAGCGCAGCTCAACTGTGG SEQ.ID.IN:1352	-1.5	-28.4	77.2	-24.4	-2.5	-9.3
441	AGAGCCATGGAGGCGCAGGG SEQ.ID.IN:1353	-1.5	-29.6	80.1	-24.7	-3.4	-8.8
466	GCGGGCCGCTTCCCAGAGGA SEQ.ID.IN:1354	-1.5	-33.9	86.2	-29.8	-2.6	-10.7
513	GCCCATGGTCTGGTGGCCAA SEQ.ID.IN:1355	-1.5	-31.6	84.2	-28.4	-1.5	-10.8
1301	GGGGTCCCCTGGCCTGGCCA SEQ.ID.IN:1356	-1.5	-37.7	96	-31.8	-3.6	-16.8
1404	GAAGCGTCAGCGGGGGCAGA SEQ.ID.IN:1357	-1.5	-29.3	78.9	-26	-1.8	-6.6
179	CTCCGTGTCTCAGGGCATCC SEQ.ID.IN:1358	-1.4	-30.2	84.3	-27.7	-1	-5.6
565	CCACAATCTGGAAGGAACAT SEQ.ID.IN:1359	-1.4	-21.3	61.3	-19.2	-0.4	-3.9
591	GCCAGGAAACCAGGACTCAG SEQ.ID.IN:1360	-1.4	-25.8	71.3	-23.7	-0.4	-4.4
931	TGCCTCTAGATTGGCTGGGC SEQ.ID.IN:1361	-1.4	-28.5	80.6	-24.9	-2.2	-10.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1602	CCAAACCTTGAAGATACTGA SEQ.ID.IN:1362	-1.4	-20.4	59.3	-19	0	-2.8
1632	GATTCCCCATCAAGGGGACA SEQ.ID.IN:1363	-1.4	-27.3	74.3	-21.2	-4.7	-11.2
74	TGCAGAGCAGGAAGGCCGGG SEQ.ID.IN:1364	-1.3	-28.9	77.7	-25.9	-1.7	-8.8
119	CCGTGATGATGGCCACCACG SEQ.ID.IN:1365	-1.3	-28.8	74	-25.5	0.7	-12.2
676	AAACATACACACACACATAC SEQ.ID.IN:1366	-1.3	-17.6	54.3	-16.3	0	-0.9
677	GAAACATACACACACACATA SEQ.ID.IN:1367	-1.3	-18	55	-16.7	0	-0.9
887	AAGTCTGCATTCTTAGCCCG SEQ.ID.IN:1368	-1.3	-26.1	73.3	-24.3	-0.1	-5.6
997	TCACTCCAGCTTGGGCAACA SEQ.ID.IN:1369	-1.3	-27.2	76	-24.3	-1.6	-5.8
1083	TGTAATCCCAGCTACTCAGG SEQ.ID.IN:1370	-1.3	-25.1	72	-23.8	0	-4.6
1130	GTCTCTACTAAAAATACAAA SEQ.ID.IN:1371	-1.3	-14.7	48.9	-13.4	0	-2
1175	TTGAGGCCAGGAGTTCGAGA SEQ.ID.IN:1372	-1.3	-25.9	73.9	-24.1	0	-7.7
1409	CAAGGGAAGCGTCAGCGGGG SEQ.ID.IN:1373	-1.3	-27.4	73.6	-24.4	-1.7	-5.2
1680	AAAACACACACACACACACA SEQ.ID.IN:1374	-1.3	-19.1	56.4	-17.8	0	0
43	GCTCATCACCAGGCTGTGGG SEQ.ID.IN:1375	-1.2	-29.3	82.5	-26.5	-1.5	-5.9
243	ATGTCGTTCCGGTGGGCCCT SEQ.ID.IN:1376	-1.2	-32.4	85.3	-29.4	-0.2	-11.8
631	CAGGCCCACTGTGCCCAGAG SEQ.ID.IN:1377	-1.2	-31.8	84	-28.9	-1.7	-9.1
759	CTGAAGGATTTTCTATCAAT SEQ.ID.IN:1378	-1.2	-18.3	57.3	-16.1	-0.9	-4.8
1095	GTGATACGCGCCTGTAATCC SEQ.ID.IN:1379	-1.2	-26.4	71.8	-24.7	0	-7.7
1192	CGAGGCCGGTGGATCACTTG SEQ.ID.IN:1380	-1.2	-27.7	74.7	-25.3	-1.1	-9
1403	AAGCGTCAGCGGGGGCAGAG SEQ.ID.IN:1381	-1.2	-28.7	77.9	-25.7	-1.8	-6.6
1750	TTTTTTTTTTTTGGCAGACA SEQ.ID.IN:1382	-1.2	-20.3	62.7	-19.1	0	-4
93	TTGATGACCAGCAGCGTGCT SEQ.ID.IN:1383	-1.1	-27.2	75.3	-24.2	-1.9	-8.7
227	CCCTGAGGCAGCGTTCCACG SEQ.ID.IN:1384	-1.1	-31.2	80.8	-28.3	-1.8	-5.8
362	CCACGGTGTGTGCCACACGG SEQ.ID.IN:1385	-1.1	-30.1	78.5	-25.5	-3.5	-12.6
454	CCAGAGGATCTGCAGAGCCA SEQ.ID.IN:1386	-1.1	-28	78	-24.5	-2.4	-10.3
463	GGCCGCTTCCCAGAGGATCT SEQ.ID.IN:1387	-1.1	-31.4	83.8	-28.9	-1.2	-9.8
650	ACACACACGGGCACACACAC SEQ.ID.IN:1388	-1.1	-25.5	69.8	-24.4	0	-4
678	AGAAACATACACACACACAT SEQ.ID.IN:1389	-1.1	-18.3	55.7	-17.2	0	-0.9
1087	CGCCTGTAATCCCAGCTACT SEQ.ID.IN:1390	-1.1	-28.3	76	-27.2	0	-4.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1203	CTTTGGGAGGCCGAGGCCGG SEQ.ID.IN:1391	-1.1	-31.5	81.3	-27.8	-2.5	-12.2
1316	CACAGAGAACTGGCAGGGGT SEQ.ID.IN:1392	-1.1	-25.7	73.2	-22.9	-1.7	-6.8
1601	CAAACCTTGAAGATACTGAA SEQ.ID.IN:1393	-1.1	-17.7	54.1	-16.6	0	-2.8
1697	GGTCACGGGTCTAGGAGAAA SEQ.ID.IN:1394	-1.1	-24.1	69.5	-23	0	-4
244	CATGTCGTTCCGGTGGGCCC SEQ.ID.IN:1395	-1	-32.2	84.4	-29.4	-0.2	-11.8
649	CACACACGGGCACACACACA SEQ.ID.IN:1396	-1	-26	70.4	-25	0	-4
1589	ATACTGAAGGGACCAGAAAG SEQ.ID.IN:1397	-1	-19.8	58.8	-18	-0.6	-4.5
12	GGCCAGCGCAGCTCAACTGT SEQ.ID.IN:1398	-0.9	-30.2	81.7	-26.8	-2.5	-11.2
341	CCACGAGGAAGACCAGGAAG SEQ.ID.IN:1399	-0.9	-24	65.9	-21.7	-1.3	-5.7
442	CAGAGCCATGGAGGCGCAGG SEQ.ID.IN:1400	-0.9	-29.1	78.6	-24.8	-3.4	-8.8
1629	TCCCCATCAAGGGGACATTT SEQ.ID.IN:1401	-0.9	-26.8	73.4	-21.5	-4.4	-11.1
1630	TTCCCCATCAAGGGGACATT SEQ.ID.IN:1402	-0.9	-26.8	73.4	-21.2	-4.7	-11.3
180	CCTCCGTGTCTCAGGGCATC SEQ.ID.IN:1403	-0.8	-30.2	84.3	-28.3	-1	-5.6
222	AGGCAGCGTTCCACGTCGGG SEQ.ID.IN:1404	-0.8	-30.5	80.8	-28.4	-1.2	-8.4
629	GGCCCACTGTGCCCAGAGAC SEQ.ID.IN:1405	-0.8	-31.9	84.6	-29.7	-1.3	-7.9
657	CACATACACACACACGGGCA SEQ.ID.IN:1406	-0.8	-24.8	68.2	-24	0	-4
922	ATTGGCTGGGCCAGAATTTC SEQ.ID.IN:1407	-0.8	-25.4	72.3	-22	-2.6	-12.1
1302	AGGGGTCCCCTGGCCTGGCC SEQ.ID.IN:1408	-0.8	-37	95.7	-31.8	-3.6	-16.8
1309	AACTGGCAGGGGTCCCCTGG SEQ.ID.IN:1409	-0.8	-31.4	83.6	-26.5	-4.1	-14.3
1631	ATTCCCCATCAAGGGGACAT SEQ.ID.IN:1410	-0.8	-26.7	73	-21.2	-4.7	-10.9
355	GTGTGCCACACGGCCCACGA SEQ.ID.IN:1411	-0.7	-32.1	81.4	-29.9	-0.4	-11
451	GAGGATCTGCAGAGCCATGG SEQ.ID.IN:1412	-0.7	-26.5	75.4	-24.3	3.4	-11.1
569	CCCACCACAATCTGGAAGGA SEQ.ID.IN:1413	-0.7	-26	70.1	-23.6	-1.7	-6
606	CACGCGCAGCAGGCTGCCAG SEQ.ID.IN:1414	-0.7	-31.7	82.2	-27.8	-2.7	-14.2
697	GCAGGAATCCAAGGGGCTAA SEQ.ID.IN:1415	-0.7	-25.3	70.3	-24	-0.3	-6.9
1125	TACTAAAAATACAAAAATTA SEQ.ID.IN:1416	-0.7	-9.3	38.4	-8.6	0	-3.2
1132	CCGTCTCTACTAAAAATACA SEQ.ID.IN:1417	-0.7	-18.9	56.6	-18.2	0	-2.6
1140	TGGTGAACCCGTCTCTACTA SEQ.ID.IN:1418	-0.7	-25.6	72	-24	-0.7	-5.4
464	GGGCCGCTTCCCAGAGGATC SEQ.ID.IN:1419	-0.6	-31.7	84.4	-29.7	-1.2	-9.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
511	CCATGGTCTGGTGGCCAAGG SEQ.ID.IN:1420	-0.6	-29	79.4	-26.3	-2.1	-10.4
517	CTTGGCCCATGGTCTGGTGG SEQ.ID.IN:1421	-0.6	-30	82.8	-28.4	-0.9	-7.9
602	CGCAGCAGGCTGCCAGGAAA SEQ.ID.IN:1422	-0.6	-28.6	75.8	-25.1	-2.5	-13.5
674	ACATACACACACACATACAC SEQ.ID.IN:1423	-0.6	-19.9	59.6	-19.3	0	-0.9
891	TGAAAAGTCTGCATTCTTAG SEQ.ID.IN:1424	-0.6	-18.7	58.3	-17.6	-0.2	-6.5
1501	CTTGGGAGGAGAAGGCTGAG SEQ.ID.IN:1425	-0.6	-24.2	70.3	-23.6	0	-3.7
1597	CCTTGAAGATACTGAAGGGA SEQ.ID.IN:1426	-0.6	-21.2	62.2	-19.9	-0.5	-4.9
1681	GAAAACACACACACACACAC SEQ.ID.IN:1427	-0.6	-19	56.4	-18.4	0	0
1288	CTGGCCATCACAGGGACTCA SEQ.ID.IN:1428	-0.5	-27.8	77.6	-26.5	-0.3	-8.9
237	TTCCGGTGGGCCCTGAGGCA SEQ.ID.IN:1429	-0.4	-33.1	86.5	-29.4	-3.3	-12.2
618	CCCAGAGACCCACACGCGCA SEQ.ID.IN:1430	-0.4	-31.8	79	-30.9	0	-8
655	CATACACACACACGGGCACA SEQ.ID.IN:1431	-0.4	-24.8	68.2	-24.4	0	-4
1131	CGTCTCTACTAAAAATACAA SEQ.ID.IN:1432	-0.4	-16.2	51.4	-15.8	0	-2.5
1173	GAGGCCAGGAGTTCGAGACC SEQ.ID.IN:1433	-0.4	-28	77.9	-27.1	0	-7.7
14	CTGGCCAGCGCAGCTCAACT SEQ.ID.IN:1434	-0.3	-29.9	80.1	-27	-2.5	-12.3
89	TGACCAGCAGCGTGCTGCAG SEQ.ID.IN:1435	-0.3	-29	79.3	-24.5	-3.8	-16.1
242	TGTCGTTCCGGTGGGCCCTG SEQ.ID.IN:1436	-0.3	-32.4	85.1	-30.3	-0.2	-11.8
771	CTGTTACTTTAGCTGAAGGA SEQ.ID.IN:1437	-0.3	-21.3	64.7	-20.1	-0.4	-9.3
1088	GCGCCTGTAATCCCAGCTAC SEQ.ID.IN:1438	-0.3	-29.2	78.2	-28.4	0	-7.6
1098	ATGGTGATACGCGCCTGTAA SEQ.ID.IN:1439	-0.3	-25.2	69.2	-23.2	-1.7	-7.8
1551	CACCCAAAGCTCCCGGTCCT SEQ.ID.IN:1440	-0.3	-31.8	80.5	-31.5	0	-6.2
1599	AACCTTGAAGATACTGAAGG SEQ.ID.IN:1441	-0.3	-18.9	57.1	-17.5	-1	-5.9
1633	GGATTCCCCATCAAGGGGAC SEQ.ID.IN:1442	-0.3	-27.8	75.7	-22.8	-4.7	-11.2
507	GGTCTGGTGGCCAAGGAGGC SEQ.ID.IN:1443	-0.2	-29.9	84	-27.4	-2.3	-9
568	CCACCACAATCTGGAAGGAA SEQ.ID.IN:1444	-0.2	-23.3	64.8	-21.7	-1.3	-5.7
634	ACACAGGCCCACTGTGCCCA SEQ.ID.IN:1445	-0.2	-32.3	84.2	-27.8	-4.3	-10.7
923	GATTGGCTGGGCCAGAATTT SEQ.ID.IN:1446	-0.2	-25.6	72	-22.8	-2.6	-12.1
930	GCCTCTAGATTGGCTGGGCC SEQ.ID.IN:1447	-0.2	-30.5	84.4	-28.7	-1.5	-9.8
1073	GCTACTCAGGAGGCTGAGGC SEQ.ID.IN:1448	-0.2	-27.9	80.9	-23.4	-4.3	-11.1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	TTGGGAGGAGAAGGCTGAGC						
1500	SEQ.ID.IN:1449	-0.2	-25.1	72.7	-24.9	0	-4.5
	CCGGTCCTCCACCCACTGCC						
1539	SEQ.ID.IN:1450	-0.2	-35.4	88.4	-34.2	-0.9	-5.4
	CCAGAGACCCACACGCGCAG						
617	SEQ.ID.IN:1451	-0.1	-29.8	76.3	-29.2	0	-8
	AGATTGGCTGGGCCAGAATT						
924	SEQ.ID.IN:1452	-0.1	-25.5	72	-22.8	-2.6	-12.1
	AGCTACTCAGGAGGCTGAGG						
1074	SEQ.ID.IN:1453	-0.1	-26.1	76.6	-22.5	-3.4	-14.2
	CCTCCTGGGCAACATGGTGA						
1154	SEQ.ID.IN:1454	-0.1	-28.3	77	-27.7	-0.1	-8
	GCACTTTGGGAGGCCGAGGC						
1206	SEQ.ID.IN:1455	-0.1	-30.2	81.8	-28.8	-1.2	-7.7
	ACACGGATTCCCCATCAAGG						
1637	SEQ.ID.IN:1456	-0.1	-26.5	71.2	-25.6	-0.6	-6
	GAGGCAGCGTTCCACGTCGG						
223	SEQ.ID.IN:1457	0	-29.9	79.6	-28.6	-1.2	-8.4
	GGCGGGCCGCTTCCCAGAGG						
467	SEQ.ID.IN:1458	0	-34.5	87.4	-31.9	-2.6	-11.2
	CCCATGGTCTGGTGGCCAAG						
512	SEQ.ID.IN:1459	0	-29.8	80.3	-27.8	-2	-10.8
	TTAGCTGAAGGATTTTCTAT						
763	SEQ.ID.IN:1460	0	-19.5	60.8	-18.6	-0.8	-7
	AGAGGGAGTGATGTTTTTGA						
795	SEQ.ID.IN:1461	0	-21.6	66.4	-21.6	0	-1.1
	TAGATTGGCTGGGCCAGAAT						
925	SEQ.ID.IN:1462	0	-25.1	71	-22.8	-2.3	-8.8
	CACACGGCCCACGAGGAAGA						
349	SEQ.ID.IN:1463	0.1	-27.6	71.7	-26.6	-1	-5.7
	CACAGGTGGCGGGCCGCTTC						
474	SEQ.ID.IN:1464	0.1	-32	84.1	-29.5	-2.6	-10.8
	AGGAATCCAAGGGGCTAAGA						
695	SEQ.ID.IN:1465	0.1	-23.4	66.7	-22.9	-0.3	-6.9
	CTTGAGGCCAGGAGTTCGAG						
1176	SEQ.ID.IN:1466	0.1	-26.2	74.5	-26.3	0	-6.9
	TGGCCAGCGCAGCTCAACTG						
13	SEQ.ID.IN:1467	0.2	-29	78.1	-26.8	-2.3	-12
	TCTGGCCAGCGCAGCTCAAC						
15	SEQ.ID.IN:1468	0.2	-29.4	80	-27	-2.5	-12.5
	TGTGTGCCACACGGCCCACG						
356	SEQ.ID.IN:1469	0.2	-31.5	80.1	-29.9	-1.1	-11.5
	GCAGCAGGCTGCCAGGAAAC						
601	SEQ.ID.IN:1470	0.2	-28	76.7	-25.7	-2	-12.9
	GGAATCCAAGGGGCTAAGAA						
694	SEQ.ID.IN:1471	0.2	-22.7	64.4	-22.9	0.5	-6.2
	AAAGTCTGCATTCTTAGCCC						
888	SEQ.ID.IN:1472	0.2	-24.6	71	-24.3	-0.1	-6.5
	ACAGAGAACTGGCAGGGGTC						
1315	SEQ.ID.IN:1473	0.2	-25.4	73.7	-23.9	-1.7	-6.8
	CACACACGGATTCCCCATCA						
1640	SEQ.ID.IN:1474	0.2	-27.6	73.3	-26.8	-0.9	-5.2
	TCTGCAGAGCCATGGAGGCG						
446	SEQ.ID.IN:1475	0.3	-28.5	78.2	-25	-3.4	-15.5
	GGTGGCCAAGGAGGCATCAG						
502	SEQ.ID.IN:1476	0.3	-28	78.3	-24.9	-3.4	-9.4
	CTTTAGCTGAAGGATTTTCT						
765	SEQ.ID.IN:1477	0.3	-20.8	63.7	-20.2	-0.8	-7.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1408	AAGGGAAGCGTCAGCGGGGG SEQ.ID.IN:1478	0.3	-27.9	75	-26.5	-1.7	-6
1530	CACCCACTGCCCTTTGGAGG SEQ.ID.IN:1479	0.3	-30.6	80.5	-30	-0.8	-5.4
440	GAGCCATGGAGGCGCAGGGG SEQ.ID.IN:1480	0.4	-30.8	82.3	-27.8	-3.4	-8.8
473	ACAGGTGGCGGGCCGCTTCC SEQ.ID.IN:1481	0.4	-33.3	86.4	-31.1	-2.6	-10.8
724	TGAAATGGTTCCCATCAGCC SEQ.ID.IN:1482	0.4	-25.7	71.2	-24.5	-1.5	-6
760	GCTGAAGGATTTTCTATCAA SEQ.ID.IN:1483	0.4	-20.1	61.4	-19.5	-0.9	-4.8
932	TTGCCTCTAGATTGGCTGGG SEQ.ID.IN:1484	0.4	-26.8	76.5	-25	-2.2	-10.6
1093	GATACGCGCCTGTAATCCCA SEQ.ID.IN:1485	0.4	-27.9	73.1	-27.8	0	-7.7
1289	CCTGGCCATCACAGGGACTC SEQ.ID.IN:1486	0.4	-29.1	80.1	-27.7	-1.8	-8.9
1306	TGGCAGGGGTCCCCTGGCCT SEQ.ID.IN:1487	0.4	-35.7	93.4	-30.5	-5.6	-16.8
1490	AAGGCTGAGCTTCCTGTGGG SEQ.ID.IN:1488	0.4	-27.5	78.1	-27.2	-0.4	-8.5
1576	CAGAAAGTTCCTTTGAGTGG SEQ.ID.IN:1489	0.4	-21.7	64.8	-21.2	-0.7	-4.1
1600	AAACCTTGAAGATACTGAAG SEQ.ID.IN:1490	0.4	-17	53	-17.4	0	-2.8
1682	AGAAAACACACACACACACA SEQ.ID.IN:1491	0.4	-18.8	56.1	-19.2	0	0
25	GGCAGGCATCTCTGGCCAGC SEQ.ID.IN:1492	0.5	-31.5	88	-29.2	-2.8	-11.9
443	GCAGAGCCATGGAGGCGCAG SEQ.ID.IN:1493	0.5	-29.7	80.4	-27.6	-2.6	-9.4
679	AAGAAACATACACACACACA SEQ.ID.IN:1494	0.5	-17.6	54	-18.1	0	-0.9
890	GAAAAGTCTGCATTCTTAGC SEQ.ID.IN:1495	0.5	-20.5	62.5	-21	0	-6.5
1128	CTCTACTAAAAATACAAAAA SEQ.ID.IN:1496	0.5	-11.7	42.7	-12.2	0	-1.2
1378	AGCCCTGTCCTTGGCTCACC SEQ.ID.IN:1497	0.5	-32.5	88.1	-30.9	-2.1	-6.5
124	TTGGCCCGTGATGATGGCCA SEQ.ID.IN:1498	0.6	-30	78.5	-26.6	-4	-10.5
342	CCCACGAGGAAGACCAGGAA SEQ.ID.IN:1499	0.6	-26	69	-25.2	-1.3	-6
526	ACGGCGGCTCTTGGCCCATG SEQ.ID.IN:1500	0.6	-31.8	81.8	-30.6	-1.8	-9.3
1190	AGGCCGGTGGATCACTTGAG SEQ.ID.IN:1501	0.6	-26.9	75.2	-26.3	-1.1	-9
1193	CCGAGGCCGGTGGATCACTT SEQ.ID.IN:1502	0.6	-29.7	78.2	-28.7	-1.6	-9
6	CGCAGCTCAACTGTGGGTGT SEQ.ID.IN:1503	0.7	-27.5	77.3	-26.4	-1.8	-7.1
8	AGCGCAGCTCAACTGTGGGT SEQ.ID.IN:1504	0.7	-28.1	78.7	-26.3	-2.5	-8.5
673	CATACACACACACATACACA SEQ.ID.IN:1505	0.7	-20.4	60.3	-21.1	0	-0.9
885	GTCTGCATTCTTAGCCCGGG SEQ.ID.IN:1506	0.7	-29.2	80.6	-29	-0.1	-9.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1133	CCCGTCTCTACTAAAAATAC SEQ.ID.IN:1507	0.7	-20.2	58.9	-20.9	0	-2.6
1290	GCCTGGCCATCACAGGGACT SEQ.ID.IN:1508	0.7	-30.5	82.7	-28.7	-2.5	-8.8
348	ACACGGCCCACGAGGAAGAC SEQ.ID.IN:1509	0.8	-27.1	71.2	-26.8	-1	-6.2
592	TGCCAGGAAACCAGGACTCA SEQ.ID.IN:1510	0.8	-25.8	70.9	-25.9	-0.4	-4.4
1089	CGCGCCTGTAATCCCAGCTA SEQ.ID.IN:1511	0.8	-29.8	77.3	-30.1	0	-7.6
1151	CCTGGGCAACATGGTGAACC SEQ.ID.IN:1512	0.8	-26.5	71.8	-27.3	0	-7.2
1691	GGGTCTAGGAGAAAACACAC SEQ.ID.IN:1513	0.8	-20.9	62.2	-21.7	0	-4
1696	GTCACGGGTCTAGGAGAAAA SEQ.ID.IN:1514	0.8	-22.2	64.8	-23	0	-4
926	CTAGATTGGCTGGGCCAGAA SEQ.ID.IN:1515	0.9	-26	73	-24.3	-2.6	-9.1
1099	TATGGTGATACGCGCCTGTA SEQ.ID.IN:1516	0.9	-25.6	70.8	-24.8	-1.7	-7.8
1196	AGGCCGAGGCCGGTGGATCA SEQ.ID.IN:1517	0.9	-31.5	82.3	-29.8	-2.5	-12.2
432	GAGGCGCAGGGGAGCTGGGC SEQ.ID.IN:1518	1	-32	86.9	-28.4	-4.6	-9.2
450	AGGATCTGCAGAGCCATGGA SEQ.ID.IN:1519	1.1	-26.5	75.4	-26.1	3.4	-11.1
593	CTGCCAGGAAACCAGGACTC SEQ.ID.IN:1520	1.1	-26	71.7	-26.4	-0.4	-4.4
937	CAGGCTTGCCTCTAGATTGG SEQ.ID.IN:1521	1.1	-26.3	75.5	-25.8	-1.6	-8.9
1094	TGATACGCGCCTGTAATCCC SEQ.ID.IN:1522	1.1	-27.2	72	-28.3	0	-7
28	GTGGGCAGGCATCTCTGGCC SEQ.ID.IN:1523	1.2	-31.4	88.2	-31	-1.5	-7.2
1082	GTAATCCCAGCTACTCAGGA SEQ.ID.IN:1524	1.2	-25.7	73.5	-26.9	0	-4.6
1153	CTCCTGGGCAACATGGTGAA SEQ.ID.IN:1525	1.2	-25.6	71.2	-26.3	-0.1	-6.9
1202	TTTGGGAGGCCGAGGCCGGT SEQ.ID.IN:1526	1.2	-31.8	82.8	-30.4	-2.5	-12.2
1278	CAGGGACTCACATGGGAGCC SEQ.ID.IN:1527	1.2	-27.6	77.1	-27.5	-1.2	-9.5
11	GCCAGCGCAGCTCAACTGTG SEQ.ID.IN:1528	1.3	-29	79	-27.8	-2.5	-9.1
27	TGGGCAGGCATCTCTGGCCA SEQ.ID.IN:1529	1.3	-30.9	85.3	-29.6	-2.6	-8.6
88	GACCAGCAGCGTGCTGCAGA SEQ.ID.IN:1530	1.3	-29.6	80.8	-26.9	-3.8	-15.3
445	CTGCAGAGCCATGGAGGCGC SEQ.ID.IN:1531	1.3	-29.9	80.7	-27.8	-3.4	-13.7
462	GCCGCTTCCCAGAGGATCTG SEQ.ID.IN:1532	1.3	-30.2	81.1	-29.3	-2.2	-8
465	CGGGCCGCTTCCCAGAGGAT SEQ.ID.IN:1533	1.3	-32.1	82.1	-31.7	-1.7	-9.8
635	CACACAGGCCCACTGTGCCC SEQ.ID.IN:1534	1.3	-32.3	84.2	-29.3	-4.3	-10.7
877	TCTTAGCCCGGGATTCAGAT SEQ.ID.IN:1535	1.3	-26.5	74	-26.6	0	-10.3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	ACTCAAACCTTGGGAGGAGA						
1509	SEQ.ID.IN:1536	1.3	-23.4	67.1	-23.1	-1.6	-6.7
	GACTCAAACCTTGGGAGGAG						
1510	SEQ.ID.IN:1537	1.3	-23.4	67.1	-23.1	-1.6	-6.6
	GCCCACGAGGAAGACCAGGA						
343	SEQ.ID.IN:1538	1.4	-28.5	74.9	-28.5	-1.3	-6
	GGCGGCTCTTGGCCCATGGT						
524	SEQ.ID.IN:1539	1.4	-33.2	87.8	-32.3	-2.3	-9.3
	GCTGCCAGGAAACCAGGACT						
594	SEQ.ID.IN:1540	1.4	-27.4	74.2	-28.1	-0.4	-4.7
	GGCTGCCAGGAAACCAGGAC						
595	SEQ.ID.IN:1541	1.4	-27.7	74.8	-28.1	-0.2	-9.8
	TCTGTTACTTTAGCTGAAGG						
772	SEQ.ID.IN:1542	1.4	-21.1	64.8	-21.6	-0.4	-9.3
	CCAGCTACTCAGGAGGCTGA						
1076	SEQ.ID.IN:1543	1.4	-27.6	78.4	-26.5	-2.5	-9.9
	TCTACTAAAAATACAAAAAT						
1127	SEQ.ID.IN:1544	1.4	-10.8	41.1	-12.2	0	-1.2
	GGCAGGGGTCCCCTGGCCTG						
1305	SEQ.ID.IN:1545	1.4	-35.7	93.4	-32.2	-4.9	-16
	AGAAGGCTGAGCTTCCTGTG						
1492	SEQ.ID.IN:1546	1.4	-25.7	74.4	-25.5	-1.6	-6.1
	GGAGGAGAAGGCTGAGCTTC						
1497	SEQ.ID.IN:1547	1.4	-25.2	74	-25.3	-1.2	-6
	GTGTGTGCCACACGGCCCAC						
357	SEQ.ID.IN:1548	1.5	-31.9	83.9	-29.9	-3.5	-14
	CACTCCAGCTTGGGCAACAG						
996	SEQ.ID.IN:1549	1.5	-26.8	74.6	-26.7	-1.6	-6.4
	CAGCTACTCAGGAGGCTGAG						
1075	SEQ.ID.IN:1550	1.5	-25.6	75	-23.2	-3.9	-12.2
	AGGCCAGGAGTTCGAGACCC						
1172	SEQ.ID.IN:1551	1.5	-29.4	80.1	-30.4	0	-7.7
	CAGAGAACTGGCAGGGGTCC						
1314	SEQ.ID.IN:1552	1.5	-27.2	76.8	-27.8	-0.8	-6.3
	CGGGTCTAGGAGAAAACACA						
1692	SEQ.ID.IN:1553	1.5	-21.5	62.1	-23	0	-3.4
	CCATGTCGTTCCGGTGGGCC						
245	SEQ.ID.IN:1554	1.6	-32.2	84.4	-33.3	-0.1	-6.6
	CCACACGGCCCACGAGGAAG						
350	SEQ.ID.IN:1555	1.6	-29	73.7	-30	-0.3	-6.2
	CAGGACTCAGGGCCCACCAC						
581	SEQ.ID.IN:1556	1.6	-30.7	82	-30.6	-1.3	-11.3
	GCAGGCTGCCAGGAAACCAG						
598	SEQ.ID.IN:1557	1.6	-28.2	75.9	-28.4	-1	-10.4
	ACGCGCCTGTAATCCCAGCT						
1090	SEQ.ID.IN:1558	1.6	-30.3	78.4	-31.3	0	-8.5
	TTGGCCCATGGTCTGGTGGC						
516	SEQ.ID.IN:1559	1.7	-30.9	85.3	-31.5	-1	-7.4
	GCTTGCCTCTAGATTGGCTG						
934	SEQ.ID.IN:1560	1.7	-27.1	77.7	-26.6	-2.2	-10.6
	AGGCTTGCCTCTAGATTGGC						
936	SEQ.ID.IN:1561	1.7	-27.4	78.9	-27.5	-1.5	-9.6
	GGCCGAGGCCGGTGGATCAC						
1195	SEQ.ID.IN:1562	1.7	-31.7	82.5	-31	-2.3	-11.8
	GAGGCCGAGGCCGGTGGATC						
1197	SEQ.ID.IN:1563	1.7	-31.4	82.6	-30.5	-2.5	-12.2
	AGGAGAAGGCTGAGCTTCCT						
1495	SEQ.ID.IN:1564	1.7	-26.3	75.6	-26.4	-1.6	-7.1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1503	ACCTTGGGAGGAGAAGGCTG SEQ.ID.IN:1565	1.7	-25.8	73	-25.9	-1.6	-6.6
667	CACACACATACACATACACA SEQ.ID.IN:1566	1.8	-20.4	60.3	-22.2	0	-0.9
995	ACTCCAGCTTGGGCAACAGA SEQ.ID.IN:1567	1.8	-26.7	74.9	-26.9	-1.6	-6.4
1091	TACGCGCCTGTAATCCCAGC SEQ.ID.IN:1568	1.8	-29.1	76.1	-30.3	0	-8.5
1636	CACGGATTCCCCATCAAGGG SEQ.ID.IN:1569	1.8	-27.5	73	-27.7	-1.6	-8.2
347	CACGGCCCACGAGGAAGACC SEQ.ID.IN:1570	1.9	-28.9	73.8	-29.5	-1.2	-6.6
583	ACCAGGACTCAGGGCCCACC SEQ.ID.IN:1571	1.9	-32	84.4	-32.3	-0.2	-11.3
1092	ATACGCGCCTGTAATCCCAG SEQ.ID.IN:1572	1.9	-27.3	72.2	-28.7	0	-7.7
1126	CTACTAAAAATACAAAAATT SEQ.ID.IN:1573	1.9	-10.5	40.5	-12.4	0	-2.9
228	GCCCTGAGGCAGCGTTCCAC SEQ.ID.IN:1574	2	-32.2	85.5	-31.7	-2.5	-9.6
346	ACGGCCCACGAGGAAGACCA SEQ.ID.IN:1575	2	-28.9	73.8	-28.6	-2.3	-7.9
935	GGCTTGCCTCTAGATTGGCT SEQ.ID.IN:1576	2	-28.3	80.6	-28.7	-1.5	-9.9
1152	TCCTGGGCAACATGGTGAAC SEQ.ID.IN:1577	2	-24.9	69.9	-26.4	-0.1	-6.9
1188	GCCGGTGGATCACTTGAGGC SEQ.ID.IN:1578	2	-28.7	79.2	-29.3	-1.3	-7.1
345	CGGCCCACGAGGAAGACCAG SEQ.ID.IN:1579	2.1	-28.7	73.6	-28.6	-2.2	-7.9
762	TAGCTGAAGGATTTTCTATC SEQ.ID.IN:1580	2.1	-19.8	61.9	-21.4	-0.1	-7
1155	CCCTCCTGGGCAACATGGTG SEQ.ID.IN:1581	2.1	-29.7	79	-30.4	-1.3	-5.3
1528	CCCACTGCCCTTTGGAGGGA SEQ.ID.IN:1582	2.1	-31.5	82.6	-30.4	-3.2	-8.7
1687	CTAGGAGAAAACACACACAC SEQ.ID.IN:1583	2.1	-18.7	56.6	-20.8	0	-3
7	GCGCAGCTCAACTGTGGGTG SEQ.ID.IN:1584	2.2	-28.1	78.2	-27.8	-2.5	-8.7
123	TGGCCCGTGATGATGGCCAC SEQ.ID.IN:1585	2.2	-30.1	78.8	-28.3	-4	-10.4
881	GCATTCTTAGCCCGGGATTC SEQ.ID.IN:1586	2.2	-27.8	77	-28.8	0	-10.3
927	TCTAGATTGGCTGGGCCAGA SEQ.ID.IN:1587	2.2	-27.1	77.1	-26.7	-2.6	-12.2
633	CACAGGCCCACTGTGCCCAG SEQ.ID.IN:1588	2.3	-32.1	84	-31	-3.4	-9
1591	AGATACTGAAGGGACCAGAA SEQ.ID.IN:1589	2.3	-21.1	62	-23.4	0.3	-4.5
92	TGATGACCAGCAGCGTGCTG SEQ.ID.IN:1590	2.4	-27.1	74.8	-25.9	-3.6	-12.2
246	TCCATGTCGTTCCGGTGGGC SEQ.ID.IN:1591	2.4	-30.6	82.9	-32.1	-0.7	-6.6
449	GGATCTGCAGAGCCATGGAG SEQ.ID.IN:1592	2.4	-26.5	75.4	-27.7	4.2	-10.4
596	AGGCTGCCAGGAAACCAGGA SEQ.ID.IN:1593	2.4	-27.5	74.5	-28.6	-0.4	-10.4

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
597	CAGGCTGCCAGGAAACCAGG SEQ.ID.IN:1594	2.4	-27.6	74.3	-28.8	-0.3	-10.4
661	CATACACATACACACACACG SEQ.ID.IN:1595	2.4	-20.5	59.7	-22.9	0	-3
878	TTCTTAGCCCGGGATTCAGA SEQ.ID.IN:1596	2.4	-26.6	74.4	-27.8	0	-10.3
672	ATACACACACACATACACAT SEQ.ID.IN:1597	2.5	-19.7	59.1	-22.2	0	-0.9
1308	ACTGGCAGGGGTCCCCTGGC SEQ.ID.IN:1598	2.5	-33.9	90.8	-33	-3.4	-13.6
693	GAATCCAAGGGGCTAAGAAA SEQ.ID.IN:1599	2.6	-20.8	60.2	-22.9	-0.1	-3.7
1639	ACACACGGATTCCCCATCAA SEQ.ID.IN:1600	2.6	-26.2	70.1	-27.8	-0.9	-5.2
1695	TCACGGGTCTAGGAGAAAAC SEQ.ID.IN:1601	2.6	-21.2	62.3	-23.8	0	-4
632	ACAGGCCCACTGTGCCCAGA SEQ.ID.IN:1602	2.7	-32	84.3	-32.8	-1.9	-9.1
681	CTAAGAAACATACACACACA SEQ.ID.IN:1603	2.7	-17.3	53.5	-20	0	-1.4
1156	ACCCTCCTGGGCAACATGGT SEQ.ID.IN:1604	2.7	-29.9	79.8	-30.4	-2.2	-9.5
1508	CTCAAACCTTGGGAGGAGAA SEQ.ID.IN:1605	2.7	-22.5	64.5	-23.6	-1.6	-5.8
582	CCAGGACTCAGGGCCCACCA SEQ.ID.IN:1606	2.8	-32.5	84.7	-33.6	-1.3	-11.3
611	ACCCACACGCGCAGCAGGCT SEQ.ID.IN:1607	2.8	-32.3	82.3	-32.7	-2.4	-8.1
696	CAGGAATCCAAGGGGCTAAG SEQ.ID.IN:1608	2.8	-23.5	66.6	-25.7	-0.3	-6.9
1081	TAATCCCAGCTACTCAGGAG SEQ.ID.IN:1609	2.8	-24.5	70.5	-26.8	-0.2	-4.7
1169	CCAGGAGTTCGAGACCCTCC SEQ.ID.IN:1610	2.8	-29.7	80	-30.9	-1.5	-7.8
26	GGGCAGGCATCTCTGGCCAG SEQ.ID.IN:1611	2.9	-30.9	86	-31.3	-2.5	-11.6
75	CTGCAGAGCAGGAAGGCCGG SEQ.ID.IN:1612	2.9	-28.6	77.1	-29.4	-2	-11.7
122	GGCCCGTGATGATGGCCACC SEQ.ID.IN:1613	2.9	-32.1	82.1	-31.7	-3.3	-9.1
1134	ACCCGTCTCTACTAAAAATA SEQ.ID.IN:1614	2.9	-20.2	58.9	-23.1	0	-2.6
1489	AGGCTGAGCTTCCTGTGGGC SEQ.ID.IN:1615	2.9	-30	85.5	-32.1	-0.5	-8.5
1507	TCAAACCTTGGGAGGAGAAG SEQ.ID.IN:1616	2.9	-21.6	62.9	-23.6	-0.7	-5.5
1529	ACCCACTGCCCTTTGGAGGG SEQ.ID.IN:1617	2.9	-31.1	81.9	-31.2	-2.8	-8.8
1596	CTTGAAGATACTGAAGGGAC SEQ.ID.IN:1618	2.9	-19.4	59	-22.3	0	-2.5
30	CTGTGGGCAGGCATCTCTGG SEQ.ID.IN:1619	3	-28.5	81.7	-29.7	-1.8	-5.5
612	GACCCACACGCGCAGCAGGC SEQ.ID.IN:1620	3	-32	81.8	-32.6	-2.4	-8.1
889	AAAAGTCTGCATTCTTAGCC SEQ.ID.IN:1621	3	-21.9	65	-24.4	-0.1	-6.5
1194	GCCGAGGCCGGTGGATCACT SEQ.ID.IN:1622	3	-31.4	81.9	-32.1	-2.3	-10.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1693	ACGGGTCTAGGAGAAAACAC SEQ.ID.IN:1623	3	-21	61.5	-24	0	-4
358	GGTGTGTGCCACACGGCCCA SEQ.ID.IN:1624	3.1	-32.9	85.7	-31.7	-4.3	-14
525	CGGCGGCTCTTGGCCCATGG SEQ.ID.IN:1625	3.1	-32.8	83.6	-33.6	-2.3	-9.3
623	CTGTGCCCAGAGACCCACAC SEQ.ID.IN:1626	3.1	-29.8	79.5	-31.8	-1	-4.8
665	CACACATACACATACACACA SEQ.ID.IN:1627	3.1	-20.4	60.3	-23.5	0	-0.9
668	ACACACACATACACATACAC SEQ.ID.IN:1628	3.1	-19.9	59.6	-23	0	-0.9
1080	AATCCCAGCTACTCAGGAGG SEQ.ID.IN:1629	3.1	-26	73.6	-28.6	-0.2	-5.2
1201	TTGGGAGGCCGAGGCCGGTG SEQ.ID.IN:1630	3.1	-31.7	82.2	-32.2	-2.5	-12.2
239	CGTTCCGGTGGGCCCTGAGG SEQ.ID.IN:1631	3.2	-32.6	84.2	-34.4	-0.2	-10.8
240	TCGTTCCGGTGGGCCCTGAG SEQ.ID.IN:1632	3.2	-31.8	83.5	-33.5	-0.2	-11
448	GATCTGCAGAGCCATGGAGG SEQ.ID.IN:1633	3.2	-26.5	75.4	-28.3	0	-10.7
616	CAGAGACCCACACGCGCAGC SEQ.ID.IN:1634	3.2	-29.6	77	-31.4	-1.3	-8
1506	CAAACCTTGGGAGGAGAAGG SEQ.ID.IN:1635	3.2	-22.4	63.9	-24	-1.6	-6.4
1577	CCAGAAAGTTCCTTTGAGTG SEQ.ID.IN:1636	3.2	-22.5	66	-24.8	-0.7	-4.3
241	GTCGTTCCGGTGGGCCCTGA SEQ.ID.IN:1637	3.3	-33	86.7	-34.5	-0.2	-11.8
361	CACGGTGTGTGCCACACGGC SEQ.ID.IN:1638	3.3	-29.9	79.3	-28.9	-4.3	-13.4
599	AGCAGGCTGCCAGGAAACCA SEQ.ID.IN:1639	3.3	-28.2	75.9	-29.7	-1.8	-10.4
664	ACACATACACATACACACAC SEQ.ID.IN:1640	3.3	-19.9	59.6	-23.2	0	-0.9
666	ACACACATACACATACACAC SEQ.ID.IN:1641	3.4	-19.9	59.6	-23.3	0	-0.9
880	CATTCTTAGCCCGGGATTCA SEQ.ID.IN:1642	3.4	-26.7	73.9	-28.9	0	-10.3
1511	GGACTCAAACCTTGGGAGGA SEQ.ID.IN:1643	3.4	-24.6	69.4	-26.4	-1.6	-6.8
238	GTTCCGGTGGGCCCTGAGGC SEQ.ID.IN:1644	3.5	-33.6	89.2	-34.9	-2.2	-11
613	AGACCCACACGCGCAGCAGG SEQ.ID.IN:1645	3.5	-30.2	78.1	-31.3	-2.4	-8
680	TAAGAAACATACACACACAC SEQ.ID.IN:1646	3.5	-16.6	52.2	-20.1	0	-0.9
682	GCTAAGAAACATACACACAC SEQ.ID.IN:1647	3.5	-18.4	56	-21.9	0	-2.8
1487	GCTGAGCTTCCTGTGGGCCC SEQ.ID.IN:1648	3.5	-32.8	89.4	-35.3	-0.1	-10
1488	GGCTGAGCTTCCTGTGGGCC SEQ.ID.IN:1649	3.5	-32	88.6	-34.8	-0.5	-7
1634	CGGATTCCCCATCAAGGGGA SEQ.ID.IN:1650	3.5	-28.4	75	-27.7	-4.2	-11.1
874	TAGCCCGGGATTCAGATGAT SEQ.ID.IN:1651	3.6	-25.7	71.3	-28.1	0	-10.3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
933	CTTGCCTCTAGATTGGCTGG SEQ.ID.IN:1652	3.6	-26.5	75.9	-27.9	-2.2	-10.6
1307	CTGGCAGGGGTCCCCTGGCC SEQ.ID.IN:1653	3.6	-35.7	93.4	-34.5	-4.8	-15.8
615	AGAGACCCACACGCGCAGCA SEQ.ID.IN:1654	3.7	-29.6	77	-30.9	-2.4	-8
928	CTCTAGATTGGCTGGGCCAG SEQ.ID.IN:1655	3.7	-27.4	77.8	-28.4	-2.6	-12.5
1168	CAGGAGTTCGAGACCCTCCT SEQ.ID.IN:1656	3.7	-28.6	78.5	-30	-2.3	-9.3
1399	GTCAGCGGGGGCAGAGGAGC SEQ.ID.IN:1657	3.7	-30.4	85.1	-33.2	-0.8	-4.7
1504	AACCTTGGGAGGAGAAGGCT SEQ.ID.IN:1658	3.7	-25.1	70.8	-27.2	-1.6	-6.6
1549	CCCAAAGCTCCCGGTCCTCC SEQ.ID.IN:1659	3.7	-33.3	83.7	-37	0	-6.2
1580	GGACCAGAAAGTTCCTTTGA SEQ.ID.IN:1660	3.7	-23.3	67.1	-26.1	-0.7	-4.3
1592	AAGATACTGAAGGGACCAGA SEQ.ID.IN:1661	3.7	-21.1	62	-24	-0.6	-4.5
1684	GGAGAAAACACACACACACA SEQ.ID.IN:1662	3.7	-19.7	58	-23.4	0	0
87	ACCAGCAGCGTGCTGCAGAG SEQ.ID.IN:1663	3.8	-29	79.8	-28.6	-3.8	-16.1
233	GGTGGGCCCTGAGGCAGCGT SEQ.ID.IN:1664	3.8	-33.6	89.4	-34.9	-2.5	-10.8
662	ACATACACATACACACACAC SEQ.ID.IN:1665	3.8	-19.9	59.6	-23.7	0	-0.9
875	TTAGCCCGGGATTCAGATGA SEQ.ID.IN:1666	3.8	-25.8	71.7	-28.4	0	-10.3
1582	AGGGACCAGAAAGTTCCTTT SEQ.ID.IN:1667	3.8	-23.9	68.7	-26.6	-1	-5.5
626	CCACTGTGCCCAGAGACCCA SEQ.ID.IN:1668	3.9	-31.6	82.2	-34.1	-1.3	-6.3
1594	TGAAGATACTGAAGGGACCA SEQ.ID.IN:1669	3.9	-21.1	61.7	-25	0	-4.5
1683	GAGAAAACACACACACACAC SEQ.ID.IN:1670	3.9	-18.7	56.1	-22.6	0	0
873	AGCCCGGGATTCAGATGATC SEQ.ID.IN:1671	4	-26.4	73.4	-29.2	0	-10.3
1189	GGCCGGTGGATCACTTGAGG SEQ.ID.IN:1672	4	-28.1	77.4	-31.4	-0.3	-8.4
1388	CAGAGGAGCCAGCCCTGTCC SEQ.ID.IN:1673	4	-31.9	86.3	-35.2	-0.4	-6.9
1496	GAGGAGAAGGCTGAGCTTCC SEQ.ID.IN:1674	4	-26	75	-29.1	-0.8	-5.8
1595	TTGAAGATACTGAAGGGACC SEQ.ID.IN:1675	4	-20.5	60.8	-24.5	0	-3.2
515	TGGCCCATGGTCTGGTGGCC SEQ.ID.IN:1676	4.1	-32.8	88.3	-34.2	-2.7	-9.1
1550	ACCCAAAGCTCCCGGTCCTC SEQ.ID.IN:1677	4.1	-31.5	81.2	-35.6	0	-6.2
624	ACTGTGCCCAGAGACCCACA SEQ.ID.IN:1678	4.2	-29.8	79.5	-32.6	-1.3	-5.6
876	CTTAGCCCGGGATTCAGATG SEQ.ID.IN:1679	4.2	-26.1	72.2	-29.4	0	-9.6
1198	GGAGGCCGAGGCCGGTGGAT SEQ.ID.IN:1680	4.2	-32.2	83.3	-33.8	-2.5	-12.2

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1493	GAGAAGGCTGAGCTTCCTGT SEQ.ID.IN:1681	4.2	-26.3	76	-28.9	-1.6	-6.5
1398	TCAGCGGGGGCAGAGGAGCC SEQ.ID.IN:1682	4.3	-31.2	84.8	-33.9	-1.6	-9.4
1505	AAACCTTGGGAGGAGAAGGC SEQ.ID.IN:1683	4.3	-23.5	66.7	-26.2	-1.6	-6.5
360	ACGGTGTGTGCCACACGGCC SEQ.ID.IN:1684	4.4	-31.2	81.6	-31.3	-4.3	-14
663	CACATACACATACACACACA SEQ.ID.IN:1685	4.4	-20.4	60.3	-24.8	0	-0.9
684	GGGCTAAGAAACATACACAC SEQ.ID.IN:1686	4.4	-19.9	59.1	-24.3	0	-3.7
1593	GAAGATACTGAAGGGACCAG SEQ.ID.IN:1687	4.4	-21.1	62	-25	-0.2	-4.5
1638	CACACGGATTCCCCATCAAG SEQ.ID.IN:1688	4.4	-26	69.9	-29.4	-0.9	-4.7
1685	AGGAGAAAACACACACACAC SEQ.ID.IN:1689	4.4	-19	57	-23.4	0	0
439	AGCCATGGAGGCGCAGGGGA SEQ.ID.IN:1690	4.5	-30.8	82.3	-31.9	-3.4	-8.8
627	CCCACTGTGCCCAGAGACCC SEQ.ID.IN:1691	4.5	-32.9	84.4	-36	-1.3	-6.3
1579	GACCAGAAAGTTCCTTTGAG SEQ.ID.IN:1692	4.5	-22.1	64.8	-25.7	-0.7	-4.3
1581	GGGACCAGAAAGTTCCTTTG SEQ.ID.IN:1693	4.5	-23.9	68.3	-27.5	-0.7	-5.6
622	TGTGCCCAGAGACCCACACG SEQ.ID.IN:1694	4.6	-29.7	77.3	-33.1	-1.1	-5.2
636	ACACACAGGCCCACTGTGCC SEQ.ID.IN:1695	4.6	-30.5	81.5	-30.8	-4.3	-10.7
669	CACACACACATACACATACA SEQ.ID.IN:1696	4.6	-20.4	60.3	-25	0	-0.9
1157	GACCCTCCTGGGCAACATGG SEQ.ID.IN:1697	4.6	-29.3	77.8	-31.7	-2.2	-9.5
1583	AAGGGACCAGAAAGTTCCTT SEQ.ID.IN:1698	4.6	-23.1	66.2	-26	-1.7	-6.2
359	CGGTGTGTGCCACACGGCCC SEQ.ID.IN:1699	4.7	-33	84.2	-33.4	-4.3	-14
761	AGCTGAAGGATTTTCTATCA SEQ.ID.IN:1700	4.7	-20.8	63.8	-24.5	-0.9	-5.4
879	ATTCTTAGCCCGGGATTCAG SEQ.ID.IN:1701	4.7	-26	73.1	-29.5	0	-10.3
1304	GCAGGGGTCCCCTGGCCTGG SEQ.ID.IN:1702	4.7	-35.7	93.4	-36.3	-4.1	-14.3
77	TGCTGCAGAGCAGGAAGGCC SEQ.ID.IN:1703	4.8	-28.4	79	-30.5	-2.7	-11.7
344	GGCCCACGAGGAAGACCAGG SEQ.ID.IN:1704	4.8	-29.1	76	-32.5	-1.3	-7.3
1694	CACGGGTCTAGGAGAAAACA SEQ.ID.IN:1705	4.8	-21.5	62.1	-26.3	0	-4
354	TGTGCCACACGGCCCACGAG SEQ.ID.IN:1706	4.9	-30.9	78.6	-33.3	-2.5	-8.6
614	GAGACCCACACGCGCAGCAG SEQ.ID.IN:1707	4.9	-29.6	77	-32.1	-2.4	-8
1513	AGGGACTCAAACCTTGGGAG SEQ.ID.IN:1708	4.9	-24	68.3	-28.4	-0.2	-5.1
1515	GGAGGGACTCAAACCTTGGG SEQ.ID.IN:1709	4.9	-25.2	70.6	-27	-3.1	-8.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1686	TAGGAGAAAACACACACACA SEQ.ID.IN:1710	4.9	-18.5	56	-23.4	0	0
670	ACACACACACATACACATAC SEQ.ID.IN:1711	5	-19.9	59.6	-24.9	0	-0.9
683	GGCTAAGAAACATACACACA SEQ.ID.IN:1712	5	-19.4	57.9	-24.4	0	-3.7
1200	TGGGAGGCCGAGGCCGGTGG SEQ.ID.IN:1713	5	-32.8	84.2	-35.5	-2.3	-11.4
1303	CAGGGGTCCCCTGGCCTGGC SEQ.ID.IN:1714	5	-35.7	93.4	-36.3	-3.4	-16.8
1397	CAGCGGGGGCAGAGGAGCCA SEQ.ID.IN:1715	5	-31.5	83.9	-33.8	-2.7	-8.5
1578	ACCAGAAAGTTCCTTTGAGT SEQ.ID.IN:1716	5	-22.7	66.7	-27.2	-0.1	-4.3
1390	GGCAGAGGAGCCAGCCCTGT SEQ.ID.IN:1717	5.1	-32.5	88	-35.7	-1.9	-7.7
1688	TCTAGGAGAAAACACACACA SEQ.ID.IN:1718	5.1	-18.9	57.3	-24	0	-4
351	GCCACACGGCCCACGAGGAA SEQ.ID.IN:1719	5.2	-30.8	77.1	-33.4	-2.6	-8.4
1389	GCAGAGGAGCCAGCCCTGTC SEQ.ID.IN:1720	5.2	-31.7	87.4	-35.7	-1.1	-6.9
1527	CCACTGCCCTTTGGAGGGAC SEQ.ID.IN:1721	5.2	-29.7	79.9	-31.7	-3.2	-8.2
438	GCCATGGAGGCGCAGGGGAG SEQ.ID.IN:1722	5.4	-30.8	82.3	-33.6	-2.6	-8.6
1170	GCCAGGAGTTCGAGACCCTC SEQ.ID.IN:1723	5.4	-29.5	80.9	-33.9	-0.9	-7.4
1392	GGGGCAGAGGAGCCAGCCCT SEQ.ID.IN:1724	5.5	-33.7	89.7	-35.2	-4	-11.8
1584	GAAGGGACCAGAAAGTTCCT SEQ.ID.IN:1725	5.6	-23.6	67.1	-27.9	-1.2	-5.2
232	GTGGGCCCTGAGGCAGCGTT SEQ.ID.IN:1726	5.7	-32.5	87.2	-34.9	-3.3	-10.8
1512	GGGACTCAAACCTTGGGAGG SEQ.ID.IN:1727	5.7	-25.2	70.6	-29.6	-1.2	-6.4
671	TACACACACACATACACATA SEQ.ID.IN:1728	5.8	-19.4	58.6	-25.2	0	-0.9
1166	GGAGTTCGAGACCCTCCTGG SEQ.ID.IN:1729	5.8	-29.1	79.4	-33.3	-1.5	-7.8
76	GCTGCAGAGCAGGAAGGCCG SEQ.ID.IN:1730	5.9	-29.2	78.8	-32.2	-2.8	-13
79	CGTGCTGCAGAGCAGGAAGG SEQ.ID.IN:1731	5.9	-26.6	74.3	-29.8	-2.7	-9.2
80	GCGTGCTGCAGAGCAGGAAG SEQ.ID.IN:1732	5.9	-27.2	76	-30.4	-2.7	-10.4
686	AGGGGCTAAGAAACATACAC SEQ.ID.IN:1733	5.9	-20.2	60	-26.1	0	-3.7
86	CCAGCAGCGTGCTGCAGAGC SEQ.ID.IN:1734	6.1	-30.6	83.6	-32.5	-3.8	-16.1
600	CAGCAGGCTGCCAGGAAACC SEQ.ID.IN:1735	6.1	-28.2	75.9	-32.7	-1.5	-9.3
1161	TCGAGACCCTCCTGGGCAAC SEQ.ID.IN:1736	6.1	-29.2	77.5	-33.1	-2.2	-8.5
1516	TGGAGGGACTCAAACCTTGG SEQ.ID.IN:1737	6.1	-24	68	-27	-3.1	-8.4
929	CCTCTAGATTGGCTGGGCCA SEQ.ID.IN:1738	6.2	-29.4	81	-33.2	-2.4	-10.2

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1167	AGGAGTTCGAGACCCTCCTG SEQ.ID.IN:1739	6.2	-27.9	77.2	-31.8	-2.3	-9.3
1129	TCTCTACTAAAAATACAAAA SEQ.ID.IN:1740	6.3	-12.8	44.9	-19.1	0	-1.2
1689	GTCTAGGAGAAAACACACAC SEQ.ID.IN:1741	6.3	-19.4	59	-25.7	0	-4
1171	GGCCAGGAGTTCGAGACCCT SEQ.ID.IN:1742	6.4	-30.3	81.6	-35.8	-0.7	-8
1514	GAGGGACTCAAACCTTGGGA SEQ.ID.IN:1743	6.4	-24.6	69.4	-28.7	-2.3	-8.2
81	AGCGTGCTGCAGAGCAGGAA SEQ.ID.IN:1744	6.5	-27.2	76	-31	-2.7	-10.7
1160	CGAGACCCTCCTGGGCAACA SEQ.ID.IN:1745	6.6	-29.5	76.8	-34.7	-1.3	-6.3
1400	CGTCAGCGGGGGCAGAGGAG SEQ.ID.IN:1746	6.6	-29.4	80	-35.5	-0.1	-4.2
685	GGGGCTAAGAAACATACACA SEQ.ID.IN:1747	6.7	-20.9	61	-27.6	0	-3.7
82	CAGCGTGCTGCAGAGCAGGA SEQ.ID.IN:1748	6.8	-28.6	79.6	-32.7	-2.7	-10.7
687	AAGGGGCTAAGAAACATACA SEQ.ID.IN:1749	6.8	-19.3	57.7	-26.1	0	-2.9
353	GTGCCACACGGCCCACGAGG SEQ.ID.IN:1750	6.9	-32.1	81.1	-36.4	-2.6	-8.7
1199	GGGAGGCCGAGGCCGGTGGA SEQ.ID.IN:1751	6.9	-33.4	85.7	-37.7	-2.5	-12.2
1494	GGAGAAGGCTGAGCTTCCTG SEQ.ID.IN:1752	7	-26.3	75.1	-31.7	-1.6	-6.5
1635	ACGGATTCCCCATCAAGGGG SEQ.ID.IN:1753	7	-28	74.3	-31.5	-3.5	-11.8
625	CACTGTGCCCAGAGACCCAC SEQ.ID.IN:1754	7.1	-29.8	79.5	-35.5	-1.3	-5.4
691	ATCCAAGGGGCTAAGAAACA SEQ.ID.IN:1755	7.1	-21.8	62.5	-28.4	-0.1	-3.7
1518	TTTGGAGGGACTCAAACCTT SEQ.ID.IN:1756	7.1	-23	66.3	-27	-3.1	-7.6
78	GTGCTGCAGAGCAGGAAGGC SEQ.ID.IN:1757	7.2	-27.6	79	-32.1	-2.7	-9.2
690	TCCAAGGGGCTAAGAAACAT SEQ.ID.IN:1758	7.2	-21.8	62.5	-28.5	-0.1	-3.7
1517	TTGGAGGGACTCAAACCTTG SEQ.ID.IN:1759	7.2	-22.9	65.9	-27	-3.1	-7.5
1519	CTTTGGAGGGACTCAAACCT SEQ.ID.IN:1760	7.2	-23.8	67.8	-28.7	-2.3	-7.3
607	ACACGCGCAGCAGGCTGCCA SEQ.ID.IN:1761	7.3	-31.9	82.4	-36.3	-2.7	-13.5
883	CTGCATTCTTAGCCCGGGAT SEQ.ID.IN:1762	7.7	-28.2	76.7	-34.7	-0.1	-10.3
1162	TTCGAGACCCTCCTGGGCAA SEQ.ID.IN:1763	7.7	-29.1	77.3	-34.6	-2.2	-9.9
229	GGCCCTGAGGCAGCGTTCCA SEQ.ID.IN:1764	7.8	-33.2	87.4	-37.7	-3.3	-8.3
884	TCTGCATTCTTAGCCCGGGA SEQ.ID.IN:1765	7.9	-28.6	78.4	-35.3	-0.1	-10.3
692	AATCCAAGGGGCTAAGAAAC SEQ.ID.IN:1766	8	-20.4	59.5	-27.9	-0.1	-3.7
1391	GGGCAGAGGAGCCAGCCCTG SEQ.ID.IN:1767	8	-32.5	86.9	-37.3	-3.2	-10.9

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	CCAAGGGGCTAAGAAACATA						
689	SEQ.ID.IN:1768	8.1	-21.1	60.7	-29.2	0	-3.7
	GGGGGCAGAGGAGCCAGCCC						
1393	SEQ.ID.IN:1769	8.1	-34	90.4	-38.9	-3.2	-10.9
	CGGTGGGCCCTGAGGCAGCG						
234	SEQ.ID.IN:1770	8.3	-33.2	85	-38.2	-3.3	-10.8
	GAGACCCTCCTGGGCAACAT						
1159	SEQ.ID.IN:1771	8.3	-28.7	77.1	-34.8	-2.2	-5.9
	GAGTTCGAGACCCTCCTGGG						
1165	SEQ.ID.IN:1772	8.3	-29.1	79.4	-35.4	-2	-8.8
	TGCCACACGGCCCACGAGGA						
352	SEQ.ID.IN:1773	8.5	-31.5	79.1	-37.4	-2.6	-8.7
	GGGCCCTGAGGCAGCGTTCC						
230	SEQ.ID.IN:1774	8.6	-33.7	89	-39	-3.3	-10
	GTTCGAGACCCTCCTGGGCA						
1163	SEQ.ID.IN:1775	8.7	-31	83.1	-37.5	-2.2	-9.9
	GGTCTAGGAGAAAACACACA						
1690	SEQ.ID.IN:1776	8.7	-20.4	60.9	-29.1	0	-4
	CCCACACGCGCAGCAGGCTG						
610	SEQ.ID.IN:1777	8.9	-32.1	81.6	-38.6	-2.4	-9.1
	ACACACACAGGCCCACTGTG						
638	SEQ.ID.IN:1778	8.9	-27.6	75.5	-33.3	-3.2	-10.1
	CACACGCGCAGCAGGCTGCC						
608	SEQ.ID.IN:1779	9	-31.9	82.4	-38	-2.5	-13.5
	TGCCCTTTGGAGGGACTCAA						
1523	SEQ.ID.IN:1780	9.1	-27.2	75.1	-33.1	-3.2	-8.7
	CTGCCCTTTGGAGGGACTCA						
1524	SEQ.ID.IN:1781	9.1	-28.8	79.5	-34.7	-3.2	-8.6
	AGCGGGGGCAGAGGAGCCAG						
1396	SEQ.ID.IN:1782	9.2	-30.8	83.3	-37.3	-2.7	-8.5
	CCGGTGGGCCCTGAGGCAGC						
235	SEQ.ID.IN:1783	9.3	-34.4	89	-40.4	-3.3	-11
	GCGGGGGCAGAGGAGCCAGC						
1395	SEQ.ID.IN:1784	9.4	-32.6	87.3	-40.1	-1.9	-7.8
	CAAGGGGCTAAGAAACATAC						
688	SEQ.ID.IN:1785	9.6	-19.3	57.7	-28.9	0	-3.7
	ACTGCCCTTTGGAGGGACTC						
1525	SEQ.ID.IN:1786	9.7	-28.3	79.1	-34.8	-3.2	-8.2
	CACTGCCCTTTGGAGGGACT						
1526	SEQ.ID.IN:1787	9.9	-28.6	78.4	-36	-2.5	-7.5
	CGGGGGCAGAGGAGCCAGCC						
1394	SEQ.ID.IN:1788	10	-32.8	86.3	-40.1	-2.7	-8.4
	AGACCCTCCTGGGCAACATG						
1158	SEQ.ID.IN:1789	10.1	-28.1	75.7	-36	-2.2	-9
	TGCATTCTTAGCCCGGGATT						
882	SEQ.ID.IN:1790	10.2	-27.4	75.2	-36.4	-0.1	-10.3
	CACACACAGGCCCACTGTGC						
637	SEQ.ID.IN:1791	10.3	-29.2	79.1	-35.2	-4.3	-10.7
	CCTTTGGAGGGACTCAAACC						
1520	SEQ.ID.IN:1792	10.3	-24.9	69.5	-32.1	-3.1	-7.6
	AGTTCGAGACCCTCCTGGGC						
1164	SEQ.ID.IN:1793	10.8	-30.3	82.5	-38.9	-2.2	-9.9
	TCCGGTGGGCCCTGAGGCAG						
236	SEQ.ID.IN:1794	10.9	-33	86.5	-40.6	-3.3	-12.2
	TGGGCCCTGAGGCAGCGTTC						
231	SEQ.ID.IN:1795	11.1	-31.7	85.5	-39.5	-3.3	-10.8
	CCACACGCGCAGCAGGCTGC						
609	SEQ.ID.IN:1796	12.2	-31.9	82.4	-41.4	-2.4	-13.1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	GCAGCGTGCTGCAGAGCAGG						
83	SEQ.ID.IN:1797	12.7	-29.8	82.8	-38.8	-3	-15.4
	AGCAGCGTGCTGCAGAGCAG						
84	SEQ.ID.IN:1798	14.3	-28.6	80.5	-38.8	-3.5	-16.1
	CAGCAGCGTGCTGCAGAGCA						
85	SEQ.ID.IN:1799	15.3	-29.3	81.2	-40.5	-3.5	-16.1
	GCCCTTTGGAGGGACTCAAA						
1522	SEQ.ID.IN:1800	17.1	-26.5	73	-40.4	-3.2	-9.6
	CCCTTTGGAGGGACTCAAAC						
1521	SEQ.ID.IN:1801	18.6	-24.9	69.5	-40.4	-3.1	-8.9

Example 15

Western blot analysis of mPGES-1 protein levels

[00186] Western blot analysis (immunoblot analysis) is carried out using standard methods. Cells are harvested 16-20 h after oligonucleotide treatment, washed once with PBS, suspended in Laemmli buffer (100 ul/well), boiled for 5 minutes and loaded on a 16% SDS-PAGE gel. Gels are run for 1.5 hours at 150 V, and transferred to membrane for western blotting. Appropriate primary antibody directed to mPGES-1 is used, with a radiolabelled or fluorescently labeled secondary antibody directed against the primary antibody species. Bands are visualized using a PHOSPHORIMAGER™ (Molecular Dynamics, Sunnyvale CA).